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FAILURE TO GROW OR THRIVE IN INFANCY.[1]

By HOWARD WILLIAMS,

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IN remembering Dr. Swift, who was an outstanding children's physician and who defined a new disease which he named erythrœdema, it is well to consider the methods he used and his approach to medical problems. Dr. Swift spent most of his active life before the era of biochemical medicine and before technical methods of investigating disease were well developed. His methods were almost entirely those of clinical observation and reasoning.

Nowadays the physician and clinical investigator often place undue emphasis on the biochemical and physiological approach to disease and tend to under-rate the methods used by Dr. Swift. Nevertheless, the clinical methods and reasoning that he used must be the basis of clinical medicine, and the foundation on which further and more complete knowledge is built. One of the greatest Australian medical discoveries, namely, that congenital malformations could be caused by disease of the fœtus, resulting from maternal rubella, was made quite recently by Gregg, using the same methods that Swift used.

The common clinical problem of growth failure illustrates the necessity for an initial clinical approach to define and elucidate the variety of problems so that the special tools and methods of the biochemist can be judiciously used.

In common clinical use the term failure to thrive means failure of normal somatic growth during infancy. In some cases the cause will be obvious, for example a gross congenital malformation, a severe feeding disorder or chronic infection. In many the cause will be hidden and revealed only by a close study of the quality of mother care, the social conditions of the family, or the function of various body systems by clinical and special methods. The purpose of this lecture is to give a broad perspective of the problem of growth failure, and to discuss especially those patients in whom the cause or causes are hidden.

To understand problems of failure of growth, it is essential to know what factors are necessary for normal growth. Although many factors are involved, they are all included in four groups. The first is a suitable

[1] The Swift Memorial Lectures, Lecture I. Delivered at Adelaide on August 26, 1958.

environment, of which mothering is by far the most important. The second is nutrition; the correct type and amount of food must be eaten, digested and absorbed. The third is utilization of the food by the tissues. Proper utilization depends on the constancy of composition of the extracellular fluid, on the correct supply of hormones by the endocrine glands, and on normal systems of intracellular enzymes. The fourth is the genotype of the organism, which must be so constituted that it is capable of normal growth. Defects or disturbances of any of these factors can either retard or arrest growth.

There are many ways in which it is possible to classify failure to thrive. The proposed classification is based partly on ætiological factors and partly on disordered physiological mechanisms. The advantage of such a classification lies in its clinical application, for it is simple and ensures that the physician will approach problems of growth failure in a thorough and systematic manner.

The causes of failure to grow may be either primarily environmental or primarily intrinsic. Primarily environmental causes include: (*a*) inadequate mother care and nutrition; (*b*) infections and infestations; (*c*) chronic intoxications. Primarily intrinsic causes include (*a*) developmental or other defects of major systems; (*b*) metabolic or enzyme deficiencies — (i) malabsorption syndromes, (ii) disturbed homœostatic mechanisms and enzyme deficiencies, (iii) endocrine deficiencies; (*c*) constitutional or genetic factors.

The physician is not infrequently consulted by anxious parents because they believe their infant is not growing at a normal rate, when in fact growth is entirely normal. It is essential to be able to assess accurately and quickly that growth is normal and the infant healthy, and also to determine the cause of the parents' anxiety about their infant's growth. With some parents this will be easy, as the worry is that the baby is smaller than the neighbour's, who is a month younger, or that growth is slower than the previous baby or than the chart in the baby book. Reassurance that the baby is perfectly healthy, that the rate of growth is often very variable in different babies, and that hereditary factors may be important is all that is required. With other parents the cause may be over-anxiety and over-protection. The source of the anxiety may be deep-seated, and time and patience are often required before the mother is able to adopt a more normal and healthy attitude to her child.

Primarily Environmental Factors.

Inadequate Mother Care and Nutrition.

As the infant's mother is the principal and most important part of his environment, it follows that the quality of the mothering and feeding he receives will be of the greatest importance in his somatic, mental and emotional health. There are many aspects of inadequate mother care. Sometimes the mother is unable to provide the right physical, nutritional or emotional care; sometimes the baby, by reason of illness or his disposition, is very difficult to mother; at times the family and social environment are inimical to both mother and baby. Any one or a combination of these factors may underlie inadequate mother care. It is well known that some babies who are kept in hospital or institutions for long periods may fail to thrive despite good physical care. If the baby's own mother or a suitable mother substitute can care for him, growth may proceed satisfactorily. The practical implication of this knowledge is that no infant should be kept in hospital without visiting by his parents, or retained in hospital when treatment can be adequately carried out at home.

Poor physical care due to ignorance can also be an important factor in failure to thrive. Among the poor socio-economic groups one may encounter infantile neglect, resulting from ignorance of the rather dull and indifferent type of mother. However, ignorance and incompetence may at times be found in mothers in the more favoured economic groups. Infants so cared for may fail to grow by reason of one or a number of factors, such as inappropriate and haphazard feeding, poor general baby care, or recurrent infection in the respiratory tract or bowel.

While inadequate physical care may be the principal factor causing growth failure in some babies, emotional deprivation or emotional disturbance may be the main cause in others. A baby may be deprived of mother love for many reasons. The illegitimate baby is frequently unwanted, just as is the unplanned baby of selfish, pleasure-seeking parents. The baby of divorced or separated parents is often brought up in an atmosphere of hostility and rejection. Career-seeking parents may find a baby comes between their personal ambitions and career, and such a baby is easily deprived of love. An over-anxious, insecure mother may transmit her emotional state to her baby, with a result that feeding difficulties and growth failure result. Anxiety and insecurity may have their origin in an immature personality, in financial or domestic problems, or in ill health of the baby or other member of the family.

In contrast to problems in which the major cause of inadequate mother care is due to the mother herself and to her social and family environment, the baby may be the major problem either by reason of illness or by disposition. Some infants get a poor start in life due to illness of the mother during pregnancy, to prematurity, to a difficult birth, to an infection or to some other illness. Such babies need special mother care, which some mothers are not able to give them without appropriate training. A common example is the baby born after a difficult labour in a hospital which is short of beds and skilled nursing care. Baby and mother are often sent home before adequate mother care and feeding are established, and not infrequently feeding difficulties and emotional disturbances develop with consequent failure to thrive. Other babies may be the alert restless type, who feed poorly, sleep fitfully and do not suck steadily or contentedly. These hyperkinetic babies often gain weight poorly, owing to low caloric intake and increased metabolic rate. The cause of this syndrome is uncertain, but genetic factors, maternal anxiety or inadequate mothering may all play a part. Associated infection or illness in the baby often aggravates the condition. These babies need special skill and patience in mothering. With suitable guidance and support most mothers learn to give the appropriate care.

It must not be assumed that all babies with what seems to be inadequate mother care fail to thrive or develop feeding difficulties or symptoms of emotional and nutritional ill health. Fortunately most infants are resilient, and many of them develop normally. The reason why one baby reacts in a totally different way to what appears to be similar mothering and environment is not always understood.

Infections and Infestations.

The sole clinical manifestation of a subacute or chronic infection may be failure to grow. This is especially so in the "hidden" infections, such as renal tract infections, primary tuberculosis, infective hepatitis without jaundice, or chronic pyæmia. Pyrexia may be absent in small weak babies, and this can mislead the inexperienced. Diagnosis of any underlying infection will be established only by systematic examination. The urine must be repeatedly examined, the chest radiologically examined, a Mantoux test done, the stool and blood cultured, and agglutination tests for brucellosis, typhoid and paratyphoid done. Malaria and kala-azar are occasionally seen nowadays in migrants.

Chronic or recurrent renal infections commonly have an underlying maldevelopment of the kidney, ureter, bladder or urethra. Appropriate investigations by micturating cysto-urethrography and pyelography are indicated. Recurrent respiratory tract or chronic infective bronchial or lung lesions may present diagnostic problems. Subacute or chronic bronchiolitis may be missed because of a radiological report that the lung fields are normal. The fact that fibrocystic disease of the pancreas may present as a bronchiolitis is not

infrequently overlooked. A collapsed infected lobe may cause few physical signs, and may be diagnosed only by the help of skiagrams of the chest.

The clinician must not assume that an infant who is failing to thrive and has a temperature must be necessarily suffering from an infection. If a thorough search has failed to disclose an infection, then other causes for the pyrexia should be considered. Emotionally disturbed infants, those with a neoplasm or reticulosis, or with pitressin-resistant diabetes insipidus may run an irregular temperature.

Worm infestations may occasionally be responsible for growth failure. *Toxascaris canis* infestation can result in irregular fever, rash, hepatic and splenic enlargement and eosinophilia. Ascaris, tapeworm and hookworm infestation may all result in failure to grow by reason of intestinal upset and poor food intake.

Toxic Agents.

Some infants or toddlers may accidentally ingest toxic agents over a period of some months and chronic poisoning may result. Chronic lead poisoning, while rare, may be suggested by an unexplained anæmia or by convulsions with a high protein content in the cerebrospinal fluid. Erythrœdema is associated with the ingestion of mercury, but the mechanism of its action is unknown. It is well to remember that irritability, refusal of food and failure to gain weight may be the initial manifestations for some weeks. Hypercalcæmia in infants is probably due either to excess vitamin D ingestion or to abnormal metabolism associated with vitamin D. The main clinical features are vomiting, hypotonicity and failure to thrive. Serum chemical examination reveals an abnormally high blood calcium content.

Other chronic poisonings are rare. The important point for the clinician to remember is that chronic intoxication should always be considered and sought as an unusual cause of failure to thrive when other causes have been excluded.

Primarily Intrinsic Factors.

Developmental or Other Defects of Major Body Systems.

Unsatisfactory growth may be the initial, and indeed the only, manifestation of a congenital defect or disease in any of the vital organ systems. Some of these systemic diseases have been considered under the heading of infections.

Central Nervous System. — Babies with cerebral lesions may present as difficult feeders. They often suck poorly, have difficulty in swallowing and frequently vomit, with the result that the total food intake is small and growth fails. The fact that feeding difficulties, particularly in the neonatal period, may be due to a cerebral cause, can easily be overlooked unless the physician is alert to the possibility. In some cases there will be definite clues of a possible cerebral cause, such as a history of difficult labour with anoxæmia, or of severe neonatal jaundice. Physical signs such as microcephaly or hydrocephalus, a tense fontanelle, or retinal anormalities will strongly indicate the likely cause of the symptoms. Unless there is some definite evidence of a cerebral lesion, diagnosis may be possible only after some months of observation, when the infant either fails to develop normal mental functions or actually exhibits signs of organic cerebral damage. Lesions such as subdural hæmatoma can be remedied by surgery, so that accurate diagnosis is essential.

Cardiovascular System. — While gross cyanotic cardiac malformations invariably result in defective growth, acyanotic lesions such as patent ductus arteriosus, coarctation of the aorta or defective atrial septum may do the same. Often the infant with patent ductus arteriosus has a systolic murmur only, but the pulses have a collapsing quality, and the systolic pressure is usually elevated with a low or even unrecordable diastolic pressure. The heart is often enlarged and the lung fields are congested.

A diagnosis of coarctation is readily established clinically by the signs of collapsing pulse, hypertension in the brachial arteries and impalpable or feeble pulses in the femoral arteries. A systolic murmur is often heard over the region of the lesion posteriorly. The heart may be large and the electrocardiogram show left ventricular hypertrophy.

The defective atrial septal defect may be suspected from a systolic precordial bruit, an enlarged right auricle, engorged lung fields and the signs of right axis strain in the electrocardiogram. Catheter studies are necessary to establish this diagnosis.

Other cardiac lesions which cause partial cardiac failure such as myocarditis or fibro-elastosis may be responsile for failure to thrive. The cardiac failure may be masked by signs of chronic or recurrent bronchitis.

Pulmonary System. — Congenital anomalies of the lungs which cause growth failure by reason of gross ventilatory defects are rare, and readily declare themselves clinically by respiratory distress and cyanosis, and radiologically by characteristic signs.

Alimentary Canal. — It is well known that lesions like pyloric stenosis cause vomiting and failure of growth, but less well appreciated that œsophageal reflux with or without hiatus hernia and œsophagitis may have the same result. Hirschsprung's disease may present with failure of growth, episodes of vomiting, severe constipation and evidence of incomplete intestinal obstruction for some months before a diagnosis can be established radiologically. Other alimentary lesions will be dealt with under malabsorption syndromes.

Bone Dystrophies. — There are a group of bone dystrophies, in which the pathology is incompletely known, but which may be declared in the early stages by growth failure. Radiological examination of the skeleton should always be undertaken in any unusual or unsolved problem of growth failure. Osteopetrosis, osteogenesis imperfecta, punctate epiphyseal dysplasia and cortical hyperostosis are among some of these disorders.

Hæmatopoietic System.—Severe anæmia from any cause may result in growth failure. The diagnosis will be established by systematic blood and marrow investigation.

Metabolic Disturbances or Specific Enzyme or Hormone Deficiencies.

1. *Malabsorption Syndromes.* — There are a group of disorders in which the passage of abnormal stools and failure to thrive are the outstanding clinical features, and steatorrhœa occurs biochemically. Fibrocystic disease of the pancreas and cœliac disease are the two commonest disorders, but anatomical abnormalities of the intestinal tract and infective hepatitis without jaundice may also give rise to these symptoms and signs. Fibrocystic disease and cœliac disease have distinctive clinical patterns, and usually a diagnosis can be readily established. The infant with fibrocystic disease as a rule fails to gain weight adequately from birth, despite a good appetite and food intake. The stools are bulky, pale, foul-smelling and frequently contain small oil droplets. The demonstration of fat droplets microscopically in the stool, after they are stained with Sudan III, is a simple, useful and fairly reliable screening test. The sweat test has proved to be a reliable diagnostic test, and has largely replaced the time-consuming duodenal intubation and enzyme estimation.

By contrast, the patient with cœliac disease thrives and makes normal progress until weaning. After the introduction of gluten-containing wheat or rye cereals, appetite fails, growth slows, the child becomes miserable, the stools become pale and loose and the abdomen distends. Any infection usually greatly aggravates the symptoms. The entire clinical and biochemical pattern is reversed if gluten is excluded from the diet, but just how gluten causes the symptoms is not understood. As this disease will cause varying degrees of ill health throughout life, the diagnosis should not be made without the support of biochemical evidence. Initially a

fat balance should be estimated and the steatorrhœa proved biochemically. The result of the sweat test is always normal in these cases.

The diagnosis of anatomical abnormalities of the intestinal tract, which cause steatorrhœa and failure to thrive, will depend on, first, establishment of the diagnosis biochemically, and secondly, investigation of the alimentary tract radiologically and bacteriologically and, if need be, by laparotomy. Stasis of intestinal contents due to disordered motor function, a blind intestinal loop and abnormal small intestinal flora may be factors causing defective digestion and absorption. Non-icteric hepatitis is suggested by an enlarged liver and spleen, a low-grade fever and contact with other cases, and biochemically by a raised serum globulin level. A liver biopsy will show compatible histological changes.

In contrast to these syndromes there is a group of toddlers who intermittently have digestive disturbances during which they lose their appetite, may vomit, and pass pale loose stools. Usually they are underweight. Steatorrhœa does not occur, and it is important to establish this biochemically. These children are often nervous and highly strung, with emotional disturbances in both mother and child. Frequently they are mistakenly diagnosed as having cœliac disease, or fat or other food intolerance, so that unusual diets are unnecessarily prescribed for them.

2. *Diseases Causing Disturbed Homœostasis.*—Claude Bernard propounded the theory that the local nutrition of tissues was dependent on the constancy of composition of the liquid *milieu intérieur*, and that the health of the body depended on those mechanisms which maintained that state. It is convenient diagnostically to consider together those diseases which result in disturbed homœostasis and failure to thrive, for the clue to the diagnosis will often be found in the demonstration of an abnormality of the extracellular fluid or of an abnormal excretion product in the urine. The more common group of disorders are renal in origin, either congenital maldevelopments, acquired diseases or enzyme defects. The main renal tubular defects are pitressin-resistant diabetes insipidus, idiopathic renal hyperchloræmia and cystine storage disease. The less common disorders of homœostasis are hepatic in origin and are dependent on enzyme deficiencies such as glycogen storage disease, galactosæmia and phenylketonuria. Clinically, disorders of homœostasis should be suspected in any cases in which infant care is adequate, no infection is present and there is no defect in any major system. Further suspicion will be roused if there is evidence of dehydration, if the liver is enlarged, or if the urine shows sugar or albumin. A serum electrolyte pattern, including estimation of sodium, potassium, calcium, chloride, alkali reserve and pH, will often yield invaluable diagnostic evidence.

In pitressin-resistant diabetes insipidus the renal tubule has the sole defect of being insensitive to pitressin, which is normally secreted. The child thus passes large quantities of dilute urine and develops a hyperosmolar type of dehydration, serum sodium levels often reaching 160 to 175 mEq/l. Vomiting, constipation and irregular pyrexia are often prominent clinical features, but these may not be observed initially. The diagnosis will be proved by demonstrating that the renal tubule is insensitive to pitressin, that other renal function is normal, and that the baby will progress if given extra water.

In idiopathic renal hyperchloræmia the carbonic anhydrase mechanism of the renal tubule fails, with the result that large amounts of bicarbonate are excreted. Chloride is retained, base is not excreted and hyperchloræmia results. The plasma bicarbonate level is low, and the urine is slightly alkaline or neutral in reaction and contains much bicarbonate. Vomiting, constipation and dehydration are prominent clinical features. Renal calcification occurs in a few cases.

Cystine storage disease is characterized by failure to grow, impairment of renal function and deposition of cystine crystals in the reticulo-endothelial system. Probably general protein metabolism is abnormal. The renal lesion is responsible for chronic dehydration, hypokalæmia, acidosis and amino-aciduria and often rickets. Diagnosis is established by demonstration of general aminoaciduria and of crystals of cystine in the bone or lymph gland reticulum cells.

Galactosæmia is due to an enzyme deficiency whereby galactose is unable to be converted into glucose. Galactose reaches a high concentration in the blood and exerts a toxic effect on all tissues. Failure to grow, mental retardation, hepatic enlargement and cirrhosis and cataracts are the main clinical features. Diagnosis depends on demonstration of galactose in the urine by chromatography or other methods.

There are several disorders of glycogen metabolism, the commonest being due to the absence of the enzyme glucose-6-phosphatase, whereby glycogen is broken down to glucose. Glycogen accumulates in the liver with resultant liver enlargement. Many of these children present clinically as failure to thrive, with an enlarged liver. Liver biopsy and demonstration of excess amounts of glycogen in the liver cells will establish the diagnosis.

Phenylketonuria is due to the absence of an enzyme in the liver which is essential for the metabolism of phenylalanine. As a result phenylalanine accumulates in the blood, cerebral function is impaired and the child fails to thrive. Diagnosis is established by the addition of ferric chloride to urine; a green colour is obtained, thereby demonstrating one of the breakdown products of phenylalanine metabolism. Chromatography will also show an intense spot for phenylalanine.

Renal failure from any cause, either congenital or acquired, may result in disturbed homœostasis and so cause failure of growth. Chemical and microscopic examination of the urine, and analysis of serum electrolytes and blood urea are the means of establishing the diagnosis. Hyponatræmia, hypokalæmia, hyperchloræmia and metabolic acidosis are some of the biochemical disorders observed.

3. *Endocrine Disorders.*—While these are uncommon causes of failure of growth, it is of great importance to establish a diagnosis, as treatment by substitution therapy is satisfactory.

If hypothyroidism is severe it is usually readily diagnosed by the characteristic features of a pale puffy face, low hair line, protruding tongue, severe constipation, subnormal temperature and sluggish mental reactions. In the milder cases the diagnosis can be difficult. Slowness in reaching normal milestones, delay of epiphyseal development and failure to grow at a normal rate should strongly suggest the possibility of hypothyroidism. The protein-bound iodine can be of real value in diagnosis of the milder case. The clinical and growth response to thyroid extract is quite striking and is an important diagnostic feature.

Gargoyles and some patients with obesity and mental retardation may be confused with cretins.

Hypoadrenocorticism may occasionally cause failure to thrive. The commonest cause is the salt-losing type of congenital adrenal hyperplasia. If the infant is a male, the diagnosis may be easily missed as there are usually no signs of virilism. If the patient is a female the abnormal external genitalia with hypertrophied clitoris and urogenital sinus strongly suggests the diagnosis. Vomiting, dehydration, hyponatræmia and elevated excretion of 17-ketosteroids in the urine establish the diagnosis.

Diabetes mellitus is an acute illness in an infant with polyuria, polydipsia and, later, vomiting and acidosis.

Hypopituitarism is a very rare disease, and the patient so affected cannot be distinguished from a genetically small infant.

Constitutional or Genetic Factors.

Some infants have a genotype of small stature, and the rate of growth is slower than the average. The diagnosis is presumptive, but is suggested if one or both parents are very small, or if there is a family history of short stature. These infants, although small, are perfectly normal and active.

Some infants in whom the gonads fail to develop do not grow at a normal rate. The majority of these infants are chromosomally males, but all have female external genitalia, uterus and fallopian tubes. Some have other defects, such as webbed neck, œdema of the hands and feet, bony defects and coarctation of the aorta. Secondary sex characteristics do not develop at puberty. The ætiology of this condition is unknown.

There are a group of children who are usually small although fully mature at birth, and whose rate of growth is slow but steady. Ossification centres appear normally, and they develop normal secondary sex characteristics. As no endocrine basis or metabolic disorder has been found for the small stature and slow growth, it is presumed that the tissues have a diminished capacity for growth. Some of these so-called primordial dwarfs have other anomalies, among which are mental retardation, mandibulo-facial dysostoses and premature senility. It is rather artificial to divide these children up into a number of separate groups.

Diagnosis.

Most of the problems of failure to grow can be solved by the basic methods of clinical medicine, namely, a complete clinical history, observation of mother and baby, a thorough physical examination and the application of simple laboratory tests. These tests include microscopic examination of the urine, bacteriological examination of body fluids, agglutination tests, Mantoux test and X-ray examination of the heart and lungs. Using these methods, the clinician will be able to establish the cause of growth failure in all the common disorders such as inadequate mother care, poor nutrition, infections or a gross defect of one of the vital organs.

As most mistakes in determining the cause of growth failure are due to lack of thoroughness in obtaining clinical evidence and of carrying out appropriate simple laboratory tests, it is pertinent to stress some of these errors. Important evidence about the possible early health of the baby will be missed unless an inquiry is made into the mother's health during pregnancy and into the circumstances of the labour. It is essential to know of any feeding problems or infections, and how the baby gained weight since birth. A family history of any growth disturbances such as small stature, or metabolic, enzyme or genetic disorders, may be of considerable importance.

Failure to observe the mother and infant together may be the reason why inadequate mother care is missed. "Hospital medicine", where the mother is often excluded from the care of her baby, can easily lead to errors of this type. Observation of mother and child is often the only way that maternal attitudes and efficiency can be assessed. It also enables an assessment of whether the infant is difficult to handle and feed or is hyperkinetic.

Failure to examine the baby systematically and thoroughly is a common mistake, largely due to lack of experience. For example, cardiac failure can easily masquerade as bronchitis, and cardiac enlargement cannot be assessed clinically in many infants. Blood pressure is difficult to record in infants, because of lack of special arm cuffs, but failure to do so may mean that the infant patent ductus arteriosus or coarctation will be missed. The infant fundus is not easily examined and requires patience, but important clues such as papillœdema, hæmorrhages and choroiditis may be the only lead to the diagnosis. A tense fontanelle or an increase in the size of the head may be the only localizing sign of a subdural hæmorrhage which is causing the baby to vomit and fail to grow. Renal examination is never complete without examination of the urine chemically and microscopically, but as it is troublesome to obtain a specimen, this test is not infrequently omitted. In alimentary lesions failure to look at the stools is a common error, merely because the baby does not pass one at the time of examination.

If thorough clinical investigation and observation and the routine radiological and laboratory tests have failed to reveal the cause of failure to thrive, then special investigations for the unusual causes will be necessary. It may be possible to obtain a lead from the clinical evidence as to whether there is any disturbed function of a system or systems. For example, a child with a bowel disturbance and abdominal distension should be investigated for a malabsorption disorder, a child with any clinical evidence of dehydration for a renal or adrenal disorder, and a child with liver enlargement for an enzyme deficiency or general liver disease. Tests for a malabsorption defect are simple and straightforward. In fibrocystic disease microscopic examination of the stool for fat globules is a useful simple screening test. Confirmatory proof will be supplied by the sweat test in almost all cases. Cœliac disease and any other suspected steatorrhœa should be investigated by a three to five day fat balance technique to confirm the clinical diagnosis. Examination of isolated stool specimens for fat can give misleading results. In cœliac disease the signs and symptoms clear when a gluten-free diet is given. If steatorrhœa is not due to cœliac or fibrocystic disease, investigation of the alimentary tract by radiological and bacteriological techniques and even laparotomy will be necessary.

Disordered states of water and electrolyte metabolism will often be suggested by disordered patterns of the serum electrolytes. For example, hypernatræmia in pitressin-resistant diabetes insipidus, hyponatræmia in salt-losing renal lesions and in hypoadrenocorticism, and hypokalæmia in cystine storage disease and some renal lesions. Hyperchloræmia occurs in lesions in which the carbonic anhydrase renal mechanism is out of order, and in some cases in which the ureters have been implanted into the colon. Detailed renal function tests will be necessary in some cases of water and electrolyte disturbances to establish a renal origin.

Chromatography is of definite but limited value in the diagnosis of growth failure. A gross general aminoaciduria is common to a number of disorders—galactosæmia, cystine storage disease, gross liver damage, lead poisoning, scurvy and nutritional rickets. In some disorders the pattern of amino-aciduria is more specific, as in phenylketonuria and galactosæmia.

Some endocrine disorders may be difficult to investigate and diagnose. The mild cretin will usually be slow to grow and have retarded epiphyseal development, a raised serum cholesterol level and a low protein-bound iodine content. The clinical response to thyroid is a valuable diagnostic tool. It is usually impossible to distinguish between hypopituitary states and genetic causes of growth retardation in infancy. Radiological examination of the skeleton should be carried out in all cases in which the cause is obscure. Some cases of osteochondro-dystrophy, metabolic rickets and reticulosis will be elucidated in this manner.

Finally, there will be a group of patients who will remain undiagnosed even after extensive and thorough investigation. Some remain small, some permanently retarded and some, quite suddenly for no apparent reason, commence to grow normally.

CHLOROTHIAZIDE: A NEW APPROACH IN THE TREATMENT OF HYPERTENSION.

By DOUGLAS STUCKEY, M.D., F.R.A.C.P.,
From the Royal North Shore Hospital, Sydney.

CHLOROTHIAZIDE ("Chlotride") has recently been introduced as a diuretic agent for oral use (Ford *et alii*, 1957; Ford *et alii*, 1958; Bayliss *et alii*, 1958; Slater and Nabarro, 1958; Laragh *et alii*, 1958; Fishman *et alii*, 1958) and has been shown to be as effective by mouth as organic mercurials are by injection (Davies and Evans, 1958). It has also been shown to potentiate the effects of numerous hypotensive agents, especially the ganglion-blocking drugs (Tapia *et alii*, 1957; Hollander and Wilkins, 1957; Freis and Wilson, 1957; Freis, Warko,

Wilson and Parrish, 1958). The following is an account of experiences in the management of hypertensive patients with this new drug.

Material and Methods.

The patients were a consecutive series from hospital and private practice, the great majority of whom had been under personal observation and treatment with chlorothiazide for at least six months. Two patients died during the period of observation, one from a ruptured gangrenous appendix (Case 5) and one from a second large myocardial infarction (Case 17). Two patients had suffered from a previous cerebral vascular accident, one from thrombosis of a posterior inferior cerebellar artery (Case 4) and one from a classical hemiplegic "stroke" (Case 7). One patient was crippled from the after-effects of severe burnt-out rheumatoid arthritis (Case 8), and one patient suffered from pulmonary emphysema of marked degree (Case 20). In two instances (Cases 1 and 10) repeated attacks of urinary tract infection had occurred earlier in life, and in these two patients the hypertension was probably renal in origin. A very strong family history of hypertension and vascular disease was noted in three patients (Cases 11, 16, 19).

Hypertensive changes in the optic fundi were graded according to the classification of Wagener and Keith (1939). The persistent presence of casts or red blood cells in the urine, together with albuminuria and elevation of the blood urea level on several occasions in the absence of congestive cardiac failure, was regarded as evidence of renal failure. Changes in the electrocardiogram were classified into four grades, and attacks of paroxysmal nocturnal dyspnœa and frank acute pulmonary œdema were recorded as evidence of left ventricular failure.

All blood pressures are casual readings taken with a standard mercury sphygmomanometer. Each average figure recorded in Table I represents a mean of the lowest readings obtained on at least three separate occasions. Pressures were measured with the patient comfortably seated or lying in bed, except that, when ganglion-blocking agents were being given, the pressures measured with the patient standing erect were recorded. With one exception, those patients with diastolic pressures of 130 millimetres of mercury or more were admitted to hospital in the first instance. A period of four to seven days' observation, during which time control readings were taken, was followed by a similar period on chlorothiazide therapy alone before other hypotensive drugs were added. After the patient's discharge from hospital, further adjustment of drug dosage was almost always necessary, and the final figures shown in Table I are those taken months later, when a reasonably steady state had been achieved. In the less severe cases all observations were made on an outpatient basis, and after an observation period of several weeks combined treatment with chlorothiazide and another drug was started. No restriction of salt intake was enforced, except that some patients in hospital had no salt added at table.

Results.

The final dosages of the various drugs used and the average blood pressure figures recorded over a period of months are shown in Table I. The assessment of the adequacy of blood pressure control has been based largely on diastolic pressures.

An example of an excellent result is seen in Case 4, that of a man, aged 44 years, who was admitted to hospital with a posterior inferior cerebellar artery thrombosis. On his admission the blood pressures were very high, grade IV changes with papilœdema were present in the optic fundi, and the blood urea level was 60 mg. per 100 ml. With reserpine together with mecamylamine in the highest doses that could be tolerated only slight control of the blood pressures could be obtained; the pressures recorded while the patient was standing were of the order of 180/120 mm. of mercury. Addition of chlorothiazide allowed the dose of ganglion-blocking agent to be reduced to a level that has produced no side effects, and for the last 12 months the blood pressure has been stable at a normal level, the patient has been symptomless and well, and a recent blood urea estimation was 33 mg. per 100 ml.

Even in Case 3, which was classed as a poor result from the point of view of blood pressure control, the patient has had consistently lower pressures since chlorothiazide was added to his régime and remains symptomless apart from some permanent impairment of his eyesight. It is now five years since his first admission to the hospital complaining of blurred vision, with very high blood pressures, gross changes in the optic fundus and papilœdema and a blood urea level of 90 mg. per 100 ml.

There has been much discussion as to whether chlorothiazide is a hypotensive agent in its own right or merely potentiates the effects of other agents.

The only case in this series in which any substantial hypotensive effect from chlorothiazide alone was observed was Case 8, that of a woman, aged 44 years, who was admitted to hospital with an attack of acute pulmonary œdema. With chlorothiazide alone, her blood pressures settled from a high level on her admission to about 140/100 mm. of mercury. On her discharge from hospital,

TABLE I.
Patients Treated with Chlorothiazide.

Case Number.	Age, (Years.)	Sex.	Changes in Optic Fundi: Grade.	Renal Failure.	Left Ventricular Failure.	Left Ventricular Preponderance. (E.C.G.)	Average Blood Pressures. (Millimetres of Mercury.)[1]		Hypotensive Therapy (Daily Dose).				Result.
							Control.	On Therapy.	Chlorothiazide. (Grammes.)	Mecamylamine. (Milligrammes.)	Reserpine. (Milligramme.)	Hydralazine. (Milligrammes.)	
1	36	M.	IV	Yes.	—	2	250/165 (193)	145/100 (115)	1·5	15	0·5	—	Fair.
2	64	F.	IV	—	—	3	270/160 (197)	130/85 (100)	1·0	20	0·75	—	Excellent.
3	54	M.	IV	Yes.	—	3	280/160 (200)	150/115 (127)	1·0	40	—	150	Poor.
4	44	M.	IV	Yes.	—	RBBB	230/145 (173)	125/85 (98)	2·0	30	—	—	Excellent.
5	54	M.	IV	Yes.	—	1	220/140 (167)	150/105 (120)	1·5	20	—	—	Fair.
6	53	M.	II	Yes.	Yes.	LBBB	220/140 (167)	140/90 (107)	1·0	30	—	—	Good.
7	73	F.	II	—	—	1	250/130 (170)	170/90 (117)	1·5	10	—	—	Good.
8	46	F.	III	—	Yes.	3	230/140 (170)	150/100 (117)	1·5	10	0·5	—	Fair.
9	63	M.	II	—	Yes.	3	240/135 (170)	120/80 (93)	1·0	30	0·5	—	Excellent.
10	43	F.	II	—	—	2	220/140 (167)	125/95 (105)	1·5	20	0·5	—	Good.
11	58	F.	II	—	—	N	220/115 (150)	130/85 (100)	1·0	5	—	—	Excellent.
12	56	F.	II	—	Yes.	3	170/110 (130)	120/85 (97)	1·0	10	—	—	Excellent.
13	47	F.	II	—	—	N	235/125 (162)	180/105 (130)	1·0	—	0·75	—	Poor.
14	44	F.	II	—	—	N	230/125 (160)	150/100 (117)	1·0	—	0·5	—	Fair.
15	50	F.	I	—	—	1	220/120 (153)	145/90 (108)	1·0	—	—	150	Good.
16	69	F.	II	—	—	1	220/125 (157)	145/95 (112)	1·0	—	—	150	Good.
17	55	F.	II	—	—	1	215/120 (152)	150/95 (113)	1·0	—	0·5	—	Good.
18	48	F.	II	—	—	N	240/110 (153)	150/80 (103)	1·0	—	—	150	Good.
19	61	F.	II	—	—	N	210/110 (143)	150/80 (103)	1·0	—	0·5	—	Good.
20	52	F.	I	—	—	RBBB	220/120 (153)	165/90 (115)	1·0	—	0·5	—	Good.

[1] Systolic and diastolic pressures are shown followed by estimated mean artrial preessures in parentheses.

the blood pressures rose to about 190/135 mm. of mercury, and it was necessary to add reserpine and mecamylamine in small dosage to achieve adequate control again.

No side effects directly attributable to chlorothiazide alone were encountered in this series. A transient rash and mild dyspepsia have been noted once each in other patients taking this drug. In those patients taking more than 1·0 gramme daily over a long period of time the serum sodium and potassium levels have been within normal limits. It seems probable that, in patients taking a reasonably normal diet, treatment with chlorothiazide in a dose of 1·0 gramme per day can be continued indefinitely without fear of potassium depletion.

A more serious side effect due to the extraordinary potentiation of the action of ganglion-blocking drugs by chlorothiazide was encountered once in this series.

In Case 1, a man, aged 36 years, with malignant hypertension, was given chlorothiazide alone in a dose of 1·5 grammes per day for one week without any substantial effect on the blood pressure. Mecamylamine in a dosage of 10 mg. per day was then added, and in two days the pressures fell to very low levels, the systolic pressure being less than 100 mm. of mercury. Almost complete suppression of urine followed, and the blood urea level, above normal limits initially, rose to a very high figure. All drugs were suspended, the blood pressures gradually rose to their former levels, urinary secretion was resumed after 48 hours and an uneventful recovery took place. The patient remained comfortable and symptomless throughout this episode, and his hypertension was subsequently controlled by the same two drugs together with reserpine in small doses.

This type of reaction has been described before (Rosenheim and Ross, 1958). As a precaution, it is recommended that in the treatment of severely hypertensive patients ganglion-blocking drugs should be added in small doses — for example, 2·5 mg. of mecamylamine twice a day, increased very gradually.

Side effects due to ganglion-blocking drugs were uncommon in this series; two patients complained of intermittent dryness of the mouth. This is one of the outstanding advantages of chlorothiazide — that the potentiating effect on the hypotensive action of ganglion-blocking drugs makes them effective in a dosage which is substantially free of side effects. The potentiating effect on other hypotensive agents allows many patients with moderately severe hypertension to be adequately controlled without the use of ganglion-blocking agents. Stability of control is another feature of chlorothiazide therapy, so that pressure readings often vary little from week to week or from month to month. This is in direct contrast to earlier régimes, in which inexplicable variations in blood pressure levels were the rule rather than the exception. A general sense of well-being has been the usual finding in these patients, again in contrast with some of the earlier drug combinations, which when effective were often accompanied by vague malaise or troublesome side effects.

Discussion.

It is clear that chlorothiazide is a most valuable addition to the drug treatment of hypertension and that in a majority of cases the blood pressure can be effectively and comfortably controlled by a combination of chlorothiazide with the ganglion-blocking drugs and other hypotensive agents. The introduction of a new and more effective therapeutic régime makes it important to reassess the aims of treatment and particularly the selection of patients for treatment. Once the decision to treat the hypertensive patient has been made and effective control of the blood pressure by drug treatment has been achieved, treatment should logically be continued for the rest of the patient's life. This decision, therefore, is not one to be taken lightly.

From a prognostic point of view it is commonly recognized that hypertensive or atherosclerotic vascular disease, particularly in the cerebral, retinal, cardiac or renal territories, is much more important than the actual levels of blood pressure recorded. It is also recognized that persistently raised pressures of sufficient degree will, in themselves, inevitably lead to progressive vascular disease. Increased peripheral resistance, which is the essential basic disorder of the hypertensive state, is reflected more accurately by mean arterial pressure (i.e., the mean pressure throughout the entire cardiac cycle, systole and diastole) than by raised systolic or diastolic pressure alone. In an individual patient, therefore, the mean arterial pressure should give a better indication of whether elevation of blood pressure *per se* is likely to produce dangerous complications, and therefore whether active treatment is justified.

Mean arterial pressures can be measured accurately only by the direct intraarterial recording of pressure pulses and their integration by graphic or electrical methods. A rough estimate may be made by adding to the diastolic pressure one-third of the pulse pressure (Wiggers, 1952; Smirk, 1957). Such a figure, based largely on diastolic pressures, but taking some cognizance of systolic pressures, may prove useful in the management of hypertensive patients. A range of estimations is set out in Table II, each horizontal line showing a number of combinations of systolic and diastolic pressures each of which gives the same estimated mean arterial pressure and which are therefore assumed to have the same significance as an assessment of the hypertensive state.

TABLE II.

Estimated Mean Arterial Pressures.

Observed Systolic and Diastolic Pressures (Mm. of Mercury).												Estimated Mean Arterial Pressure. (Mm. of Mercury.)	Classification.
170/65	160/70	150/75	140/80	130/85	120/90							100	Normal range.
	175/70	165/75	155/80	145/85	135/90	125/95						105	
		180/75	170/80	160/85	150/90	140/95	130/100					110	
			185/80	175/85	165/90	155/95	145/100	135/105				115	Slight hypertension.
				190/85	180/90	170/95	160/100	150/105	140/110			120	
					195/90	185/95	175/100	165/105	155/110	145/115		125	
						200/95	190/100	180/105	170/110	160/115	150/120	130	
215/95	205/100	195/105	185/110	175/115	165/120							135	Moderate hypertension.
	220/100	210/105	200/110	190/115	180/120	170/125						140	
		225/105	215/110	205/115	195/120	185/125	175/130					145	
			230/110	220/115	210/120	200/125	190/130	180/135				150	
				235/115	225/120	215/125	205/130	195/135				155	Severe hypertension.
				250/115	240/120	230/125	220/130	210/135	200/140			160	
					225/120	245/125	235/130	225/135	215/140	205/145		165	
						260/125	250/130	240/135	230/140	220/145		170	
265/130	255/135	245/140	235/145	225/150	215/155							175	Very severe hypertension.
	270/135	260/140	250/145	240/150	230/155	220/160						180	
			265/145	255/150	245/155	235/160						185	
				260/150	250/155	240/160	230/165					190	

It should be emphasized that estimated mean arterial pressures should not be calculated from a single casual record of systolic and diastolic pressures, but from an average of the lowest readings obtained on at least three separate occasions.

Normal Range.

By the strictest criteria, mean arterial pressures up to 100 mm. of mercury would be regarded as normal, and most practising physicians would accept up to 110 mm. of mercury as within the normal range. The only point to stress is that figures of the order of 170 mm. of mercury, systolic, and 80 mm., diastolic, commonly found in elderly persons with rigid aortas, give mean arterial pressures within the normal range.

Slight Hypertension.

Mean arterial pressures from 111 to 130 mm. of mercury are included under the heading of slight hypertension. In general, hypertension of this order seldom justifies treatment unless there are other important factors involved. In the present series the only patient in this group who was treated was a woman, aged 56 years (Case 12), who was admitted to hospital in congestive heart failure for which no cause other than hypertension could be found, and it was assumed that the blood pressures had been much higher at some earlier stage.

Moderate Hypertension.

This group, with mean arterial pressures ranging from 131 to 150 millimetres of mercury, offers the greatest difficulty in deciding about treatment. Hypertension of this order in young persons, and possibly in males at any age, should be treated. A family history of hypertension, significant symptoms, electrocardiographic changes or definite grade II hypertensive changes in the optic fundus would all influence the physician to commence treatment. On the other hand, it is well documented that many females tolerate blood pressures of this level for 20 or 30 years without developing serious complications. In the present series the two patients in this group (Cases 11 and 19) both had a strong family history of hypertension and vascular disease.

Severe Hypertension.

Estimated mean arterial pressures of more than 150 mm. of mercury are, in my opinion, an indication for active treatment independent of other findings. It seems probable that hypertension of this order will, if untreated, cause serious complications in a majority of patients. Most of the patients in the present series fell into this group and in many of them serious complications were already present.

Very Severe Hypertension.

Patients with mean arterial pressures of 170 mm. of mercury or more either have malignant hypertension or are in imminent danger of developing it, and the indications for hypotensive therapy are urgent.

General Approach to Treatment.

Apart from weight reduction in obese patients and advice against excessive salt intake, no manipulation of the diet was attempted. On the experience in the present series, most hypertensive patients with estimated mean arterial pressures less than 160 millimetres of mercury can be adequately controlled without ganglion-blocking agents, and these patients can be started at once on chlorothiazide combined with some other hypotensive drug. For patients with more severe hypertension and mean arterial pressures of 160 mm. of mercury or more, ganglion-blocking drugs will almost always be necessary to achieve adequate control. In such cases it is wise to give chlorothiazide alone for about a week and then to add a ganglion-blocking drug in small doses at first, gradually increasing every few days. Addition of another hypotensive drug to the régime may be necessary.

Assessment of Results.

Adequate control of hypertension implies the production of normal or near-normal pressures for an indefinite period of time. Estimated mean arterial pressures offer a useful yardstick, and the following scheme may be used in assessment:

Excellent	up to 100 mm. of mercury.
Good	101 to 110 mm. of mercury.
Fair	111 to 120 mm. of mercury.
Poor	121 to 130 mm. of mercury.
Unsatisfactory	more than 130 mm. of mercury.

If this method of assessment is applied to the cases in the present series, in which the results have been graded largely on diastolic pressures, the comparison is fairly good, except that in four instances (Cases 7, 16, 17 and 20) the assessment would now be "fair" instead of "good". This is probably a more accurate appraisal of the degree of control obtained.

Summary.

Experience in the use of chlorothiazide in the long-term management of 20 hypertensive patients is presented.

Chlorothiazide potentiates the effects of other hypotensive drugs, and in the majority of cases very satisfactory control of blood pressures can be achieved. In the case of ganglion-blocking drugs, lower doses may be employed with less troublesome side effects.

It is suggested that estimated mean arterial pressures may be a useful index of the hypertensive state, both in the selection of patients for treatment and in the assessment of results.

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DEVELOPMENT OF RESISTANCE TO ANTIBIOTICS BY STAPHYLOCOCCI: A COMPARATIVE STUDY USING TETRACYCLINE[1] AND OLEANDOMYCIN[2] SEPARATELY AND IN COMBINATION.[3]

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THE problem of antibiotic-resistant strains of *Staphylococcus aureus* var. *pyogenes* has become clinically urgent, and the use of antibiotic combinations is probably one of the most controversial subjects in the field of antibiotic therapy today (English *et alii*, 1956; Garrod, 1957; Oswald and Welch, 1957-1958). The emergence of resistance has been found not only with penicillin and streptomycin, but also with the tetracyclines, chloramphenicol, oleandomycin, erythromycin, novobiocin and ristocetin.

Definite evidence of the value of a combination of antibiotics in delaying emergence of resistance is now universally accepted in the case of streptomycin, isoniazid, PAS and other antituberculosis drugs. Fairbrother (1957), in failing to confirm synergism with tetracycline-oleandomycin combinations *in vitro* against *Staph. aureus*, states in his summary:

> Studies of sigmamycin (a combination of 2 parts tetracycline and 1 part oleandomycin) have confirmed claims that the mixture delays in vitro the emergence of resistant variants of Staph. aureus.

This work induced us to resume a study, begun in 1956, in which the rate of emergence of resistance *in vitro* of various staphylococcal phage types to a fixed ratio of oleandomycin and tetracycline in combination[3] was compared with the rate of emergence of resistance to each constituent alone.

Initially 12 strains had been selected by one of us, and this formed Series I of the study. This work was interrupted; but the results, comparable with those found by other workers (personal communication), were such as to influence us to resume the work with another 13 strains (Series II), making 25 in all. The two series will be dealt with separately, although the method was similar in each with one small variation as described below.

Materials and Method.

Selection of Organisms.

In Series I, 12 strains were selected to give (*a*) variable phage patterns and (*b*) variable initial sensitivity according to routine laboratory tests (disk method).

In Series II, 13 strains were selected to give variable phage patterns, but less emphasis was placed on the pattern of initial antibiotic sensitivity.

Preparation of Primary Inoculum.

Initially two subcultures on nutrient agar slopes were made from the primary culture. One of these was submitted for phage typing. If this was satisfactory, 12 ml. of glucose-veal broth were inoculated from a 24 hours old nutrient agar subculture of the other, which had been kept at room temperature pending selection. The broth culture was diluted just before use.

Stock Solutions.

Stock solutions of "Synermycin" and each of its components (oleandomycin and tetracycline) were made by dissolving 20 mg. of the antibiotic in 20 ml. of sterile distilled water (1000 μg. per millilitre). These stocks were kept in small quantities at −20° C., sufficient for each day's work being taken as required. Stock solutions were kept for no longer than one month.

Method.

The stock solution of each antibiotic, after being thawed, was diluted in glucose-veal broth to give a series of 10 tubes (three inches by three-eighths of an inch) containing 200, 100, 20, 10, 5, 2·5, 1·25, 0·625, 0·313, and 0·156 μg. These amounts of antibiotic were contained in a volume of 0·5 ml. The inoculum consisted of 0·5 ml. of a one in 10 dilution of an 18 hour broth culture of *Staph. aureus*. The final antibiotic dilutions were thus:

Tube Number	Antibiotic Dilution (Micrograms per Millilitre)
1	100
2	50
3	10
4	5
5	2·5
6	1·25
7	0·625
8	0·3
9	0·15
10	0·078

A control tube of inoculum, without antibiotic, was set up for each strain at every transfer. The tubes were incubated at 37° C. for 48 hours, and the lowest concentration of antibiotic that inhibited growth after this period was noted.

A subculture on to a blood-agar plate was made from that tube with the highest concentration of antibiotic in which growth was apparent. The plates were incubated at 37° C. overnight; then a single colony was picked off and inoculated into 12 ml. of glucose-veal broth and incubated at 37° C. for 18 hours. This culture, diluted one in 10 in glucose-veal broth, was used as the inoculum in a fresh series of titrations. The organism was regarded as resistant when it was no longer inhibited by 100 μg. per ml. Organisms recovered at this stage from Series II were again phage typed, and in all cases the strains corresponded to the original phage type.

Results and Comments.

The results are set out in Table I (Series I) and Table II (Series II).

Series I.

The outstanding feature of the first series was the fact that if an organism, already resistant to a concentration of 100 μg. per millilitre of oleandomycin and tetracycline separately, failed to become resistant to 100 μg. per millilitre of "Synermycin" within a further three or four passages, then it seemed to remain at a low level of sensitivity for many passages. This effect bore no relation to the original degree of sensitivity to oleandomycin, tetracycline and "Synermycin". It was thought that this might have been due to chance selection, and in an attempt to rule this out, a small series was taken in which more than one colony from the blood agar plate was inoculated into the inoculum broth, and results were compared with controls, prepared as described under "Methods". No difference was apparent. This variation in method was then continued.

All organisms had become resistant to 100 μg. per millilitre of oleandomycin and tetracycline by the eighth passage. In three instances the development of resistance to 100 μg. per millilitre of "Synermycin" followed after resistance had developed to oleandomycin and tetracycline separately; but this was delayed for two passages in one strain, for three passages in another, and for 14 passages in the third strain. In the remaining nine strains the minimal inhibitory concentration did not rise above 100 μg. per millilitre, even though in some cases 18 transfers were carried out. These results and impressions indicated a need for further investigation (Series II).

Series II.

The second series gave somewhat different results. Although all 13 strains had become resistant to oleandomycin after one to seven passages, only three became resistant to 100 μg. per millilitre of both oleandomycin and tetracycline separately. Of the three organisms,

[1] "Tetracyn",—the trade name of Pfizer Corporation for tetracycline hydrochloride—was used in this study.
[2] "Matromycin"—the trade name of Pfizer Corporation for oleandomycin phosphate—was used in this study.
[3] "Synermycin"—the trade name of Pfizer Corporation for tetracycline hydrochloride and oleandomycin phosphate in a 2:1 ratio. Since this study was carried out, the antibiotic "Synermycin" contains the triacetyl salt instead of the phosphate salt of oleandomycin, and this gives much higher blood levels of the latter.
[4] Working under a grant from Pfizer Corporation.

TABLE I.
Series I.

	Strain Number.											
	1	2	3	4	5	6	7	8	9	10	11	12
Phage type	80/81	3C	47	52, 52a, 80, 81	3b, 3C	73	29	3b, 3C, 55	53	42D	53, 77	52a, 80
Initial antibiotic sensitivities:												
Penicillin	R	S	R	R	S	R	S	S	R	S	R	R
Streptomycin	S	S	R	R	S	S	S	S	R	S	R	R
Chloramphenicol	S	S	S	S	R	S	S	S	S	S	S	R
Tetracycline	S	S	R	R	S	S	S	S	R	S	R	R
Initial minimal inhibitory concentration[1]:												
Oleandomycin	10·0	50·0	10·0	50·0	50·0	50·0	2·5	10·0	1·25	10·0	1·25	1·25
Tetracycline	50·0	10·0	>100·0	1·25	1·25	1·25	0·625	100·0	>100·0	10·0	>100·0	>100·0
"Synermycin"	0·625	1·25	10·0	50·0	10·0	1·25	1·25	1·25	2·5	1·25	10·0	2·5

The number of strains which developed resistance to concentrations of 100 μg. per millilitre of the test substances were as follows: oleandomycin, 12; tetracycline, 12; "Synermycin", 3. All 12 strains developed resistance to oleandomycin and tetracycline within eight passages. Of the three strains which developed resistance to this concentration of "Synermycin", one took 16 passages, one took 11 passages, and one took nine passages. The phage types were not rechecked after the original typing and selection.

[1] Microgrammes per millilitre.

Number 4 showed resistance to oleandomycin at the sixth passage and to tetracycline at the third, and after 19 transfers was inhibited by only 5 μg. per millilitre of "Synermycin"; Number 8 was resistant to oleandomycin at the sixth passage and to tetracycline at the thirteenth; at the nineteenth passage it had a minimal inhibitory concentration of 5 μg. per millilitre of "Synermycin". Number 11 similarly, with resistance to oleandomycin at the seventh passage and to tetracycline at the third, still had a minimal inhibitory concentration of 5 μg. per millilitre of "Synermycin" at the nineteenth transfer. Of the remaining 10 organisms, one, Number 7, showed resistance to oleandomycin at the fifth passage, and at the nineteenth had a minimal inhibitory concentration of 1·25 μg. per millilitre of tetracycline and 2·5 μg. per millilitre of "Synermycin". All the others (nine) showed a higher minimal inhibitory concentration for tetracycline, varying from twice to 40 times that for "Synermycin".

Although the latter high figure may be due to the dilutions used, nevertheless, after 19 passages, nine out of 10 strains showed a greater sensitivity to the combination of two antibiotics, notwithstanding the fact that the organism was resistant to the other antibiotic in the combination. This is perhaps brought out more clearly in the graph (Figure I). These results do not confirm the opinion held by some that the delay in emergence of resistance attained by the combination is merely dependent on the more effective of its two constituents.

Criticism may be levelled at the tube dilution method used in this work; but we felt justified in using it, as the problem was to compare the efficiency of the combination with the individual constituents with regard to delaying emergence of resistance, and not to study the actual mechanisms of development of resistance.

Occasionally with most strains, in progressing from one transfer to the next, the minimal inhibitory concentration decreased, and this was confirmed by repeating the transfer. This has also been found by other investigators and is still unexplained. There is a possibility that it is due merely to the effect of repeated subculture, as Barber *et alii* (1958) noted that many strains resistant to erythromycin on primary isolation became less resistant after subculture in the laboratory.

TABLE II.
Series II.

	Strain Number.												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Phage type	80/81	7/47D/ 53I	3b/3C/ 55	31B	81	52, 52a, 80, 81	Phage group 3	29	3b, 3C	29, 52, 52a	53, 73	52	29
Antibiotic sensitivities:													
Penicillin	R	R	R	R	R	R	S	S	S	S	R	S	S
Streptomycin	S	S	S	S	S	S	S	S	S	S	S	S	S
Chloramphenicol	S	S	S	S	S	R	S	S	S	S	S	S	S
Tetracycline	S	S	S	S	S	S	S	S	S	S	S	S	S
Initial minimal inhibitory concentration[1]:													
Oleandomycin	1·25	5·0	50·0	5·0	2·5	2·5	2·5	2·5	2·5	5·0	2·5	2·5	2·5
Tetracycline	1·25	1·25	1·25	5·0	5·0	0·6	1·25	1·25	1·25	1·25	50·0	1·25	0·6
"Synermycin"	0·6	0·3	1·25	1·25	5·0	0·6	0·6	0·6	0·6	0·6	2·5	0·6	0·3
Final minimal inhibitory concentration[1]:													
Oleandomycin	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100
Tetracycline	5·0	5·0	10·0	>100	10·0	5·0	1·25	>100	50·0	10·0	>100	10·0	10·0
"Synermycin"	2·5	1·25	5·0	5·0	1·25	1·25	2·5	5·0	1·25	0·6	5·0	2·5	5·0
Number of transfers required to reach final minimal inhibitory concentration[2]:													
Oleandomycin	2	2	1	6	7	6	5	6	4	1	7	3	4
Tetracycline	19	19	19	3	19	19	19	13	19	19	3	19	19
"Synermycin"	19	19	19	19	19	19	19	19	19	19	19	19	19

[1] Microgrammes per millilitre.
[2] All original phage types recovered after final transfers.

Every effort was made to keep a standard technique, and on one occasion a fresh batch of antibiotics was prepared in case there had been deterioration during storage.

This work was undertaken to observe the emergence of resistance of the organisms, but it is not without interest to note the initial minimal inhibitory concentrations of each antibiotic to the organisms. It can be seen that in nine out of the 13 the minimal inhibitory concentration of the combination is less than either of the separate constituents. This is of interest with regard to the controversial subject of "in-vitro synergism"; but in this series the figures are not statistically significant.

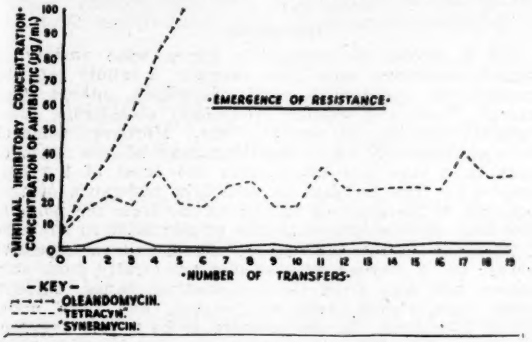

FIGURE I.

General Discussion.

This paper does not purport to establish any definite conclusions. Hundreds of transfers of organisms were carried out and the results were tabulated; this gave rise to many unanswered queries, and to some doubt as to whether previously held theories were in fact true. The recent paper by Barber *et alii* (1958) provides further evidence of the effect of combinations of antibiotics in non-tuberculous infection, specifically with regard to the emergence of resistant clinical isolates, and it gives additional evidence that much work remains to be carried out. Of the total of 25 strains in these two series, it is seen that all quickly developed resistance to oleandomycin. Twelve became resistant to tetracycline and only three to "Synermycin", the latter after at least nine transfers.

The results of these tests *in vitro* suggest that the combination of oleandomycin and tetracycline tends to delay the development of resistance by the *Staph. aureus*. These are in-vitro studies, and their clinical significance remains to be accurately assessed. It would seem, however, that further in-vivo work is warranted in the field. One of the practical questions to be answered is whether the use of a combination which delays emergence of resistant organisms would lessen the number and hence the inherent dangers of resistant staphylococci in the community. Unfortunately, the cultures after the final transfer in "Synermycin" were not tested for sensitivity to each component separately.

Summary.

Twenty-five strains of *Staph. aureus* were tested *in vitro* against increasing concentrations of oleandomycin-tetracycline, oleandomycin phosphate and tetracycline hydrochloride, in order to watch the emergence of resistance of the organisms.

Whereas resistance emerged in 100% of the strains with oleandomycin and in about 50% with tetracycline, it occurred in only 12% with oleandomycin-tetracycline, and then after a greater number of transfers as compared with its separate constitutents.

Acknowledgements.

Acknowledgement is made of help received from the staff of the Fairfax Institute of Pathology. Supplies of some equipment and antibiotics were provided by Pfizer Corporation.

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A SURVEY OF THE PENICILLIN SENSITIVITY OF STAPHYLOCOCCUS AUREUS IN GENERAL PRACTICE.[1]

RECENT INVESTIGATION into the penicillin sensitivity of *Staphylococcus aureus* has shown that in many cases a high percentage of these organisms are resistant to penicillin, and that treatment with penicillin is therefore not of great value. Frequently, and at any rate for the more serious conditions, treatment is begun primarily with the broad-spectrum antibiotics, and the results seem to be reasonably good. It was of interest, therefore, to collect from members of the New South Wales Faculty of the College of General Practitioners (now the Australian College of General Practitioners) reports of the antibiotic sensitivity of the coagulase-positive *S. aureus* from pathology reports implicating this organism gathered from patients in the members' practices.

At the same time, for purposes of comparison, similar reports were gathered from various hospitals in the Sydney metropolitan area concerning the antibiotic sensitivity of this organism.

Another Similar Investigation.

Recently, in a combined study by the Commonwealth Department of Health and the Australian College of General Practitioners, a Commonwealth-wide survey has been carried out into the same subject (to be published later). At this survey a strong point was made that the swabs taken for culture and sensitivity testing should be in all consecutive cases of soft-tissue infection, irrespective of the severity. Therefore the figures in this survey differ from those in our faculty studies, in that clinical severity and/or lack of response to treatment in no way dictated further investigation by means of a sensitivity test. This was done in the first instance prior to the institution of treatment or as soon afterwards as pus presented from the lesion.

The New South Wales Faculty Survey.

Method.

In the survey from members of the N.S.W. Faculty of the College, 337 reports were gathered. They covered both city and rural practices, and all age groups. It is stressed again that this series in no way covers consecutive cases, but rather the more severe infections or those less responsive to the initial treatment, in which case a request was made to the local hospital, laboratory or pathologist for a "culture and sensitivity test", and the result of this request forms the basis of the statements.

Results.

Sensitivity.—In the 337 reports, 79 organisms (23·4%) were stated to be sensitive to penicillin, and the remaining 258 (76·6%) resistant.

[1] An investigation carried out by the Research Committee of the New South Wales Faculty of the Australian College of General Practitioners. Recorder: W. Breinl, Hurstville, N.S.W.

Age Distribution.—The ages of the patients ranged from seven days to 80 years. Details are shown in Table I.

Sex.—The sex distribution was not significant, nor was the sensitivity related to the sexes. Details are shown in Table II.

Relation to Calendar Year.—In the distribution by years, 1954 and 1955 were very poorly represented, and the number of cases was not sufficient to be statistically

TABLE I.
Age Distribution.

Age. (Years.)	Number in Each Decade.
0 to 10	85 (25·0%)
11 to 20	41 (12·1%)
21 to 30	51 (15·0%)
31 to 40	77 (22·7%)
41 to 50	41 (12·8%)
51 to 60	24 (7·1%)
61 to 70	15 (4·4%)
71 to 80	3 (0·9%)

significant. It is of interest, however, that in 1955, of the six *S. aureus* infections, five were reported to be resistant to penicillin, and only one sensitive, which is a higher number than one would expect. Over the remaining years 1956 to 1958, the percentage of *S. aureus* infections resistant to penicillin has remained about the same, and it would appear that the organisms have not become progressively more resistant to penicillin during those

TABLE II.
Sex Distribution.

Subjects.	Sensitive Organisms.	Resistant Organisms.
Males (192—57%)	50 (26·1%)	142 (73·9%)
Females (145—43%).. ..	30 (20·6%)	115 (79·4%)

three years. Time and further investigation will show whether the number of these organisms resistant to penicillin is rising. For the moment it will remain a matter for speculation whether this finding may be due to the decreasing use of penicillin for the more obviously resistant organisms, or whether the increasing use of the broad-spectrum antibiotics is tending to eliminate the more resistant forms.

Table III illustrates this point.

TABLE III.
Sensitivity in Consecutive Calendar Years.

Year.	Number of Cases.	Sensitive Organisms.	Resistant Organisms.
1954	2	0	2
1955	6	1	5
1956	100	27 (27·0%)	73 (73·0%)
1957	120	24 (20·0%)	96 (80·0%)
1958	109	25 (22·9%)	84 (77·1%)

Influence of Case Selection.—During the Australia-wide survey carried out between the months of May and December, 1958, in the southern sector of Sydney, 102 cases of proved coagulase-positive *S. aureus* infections were encountered by myself (a participant in the investigation). It is to be stressed that under the terms of the survey these were all consecutive cases of soft-tissue infection from which swabs were gathered and cultured irrespective of clinical severity. At the conclusion of the survey it was of interest to find that of the 102 infections, 40 (39·8%) were reported to be sensitive to penicillin and the remaining 62 (60·2%) to be resistant, both in maximum and in minimum concentrations of the sensitivity disks. It would appear, therefore, that whenever patients are selected for sensitivity tests, the ratio of insensitive to sensitive organisms will rise, since the initial treatment with penicillin or sulphonamides or both will cure the infections sensitive to these agents, and the ones they do not cure will be investigated by culture and sensitivity tests as a guide to further treatment.

Comparable Figures from Hospital Practice.—The hospital series comprised 5408 infections in which the *S. aureus* was the only or the predominating organism, and of these 1384 (25·6%) were indicated to be sensitive to penicillin and 4024 (74·4%) insensitive. These results covered the period from 1954 to 1957.

Discussion.

The *S. aureus* is responsible for a wide variety of clinical conditions, some (for example, a mildly infected eczema) not producing much disability, others (for example, boils and similar conditions) occasioning some disability and loss of working time. Moreover, some of the staphylococcal lung conditions may be the cause of death in a very few hours from the onset of the first symptoms. The problem of penicillin resistance of this organism is therefore an important one from the point of view both of morbidity and also of mortality in the case of infections of internal organs. From this retrospective survey, the *S. aureus* was isolated principally from skin lesions, and also from the conjunctivæ, lungs, bladder, bowel, ears, throat, nose and vagina, and from many wound infections. It also appears to be a very frequent symptomless inhabitant of the nose and throat, and can be conveyed from there by fingers and other agencies to all parts of the body of the host and others. It appears over the years to be becoming a more frequent inhabitant of the ears, usually in a mixed infection, and would seem to be causing as many infections of the external ear as the ubiquitous fungus. Indeed, the appearance of an external meatus infected with *S. aureus* differs very little from that infected by a fungus.

Since penicillin and/or sulphonamides appear to be the first line of treatment over the years, both from their position as unrestricted National Health Service benefits and from their comparatively low cost compared with that of the broad-spectrum antibiotics, the widespread insensitivity of the staphylococcus to them is a matter for concern. This has been met to a large degree by the availability of broad-spectrum antibiotics as restricted benefits in the National Health Service for cases of proved staphylococcal causation. These substances have their own hazards and are costly, but appear to be effective both clinically and *in vitro*. So far very few strains seem to be resistant to streptomycin, "Chloromycetin", tetracyclines or erythromycin; but an occasional strain has been proved, at least *in vitro*, to be resistant to these named antibiotics, in addition to sulphonamides and penicillin. One has shown a sensitivity to neomycin only, one to "Rovamycin" only, and one to oleandomycin, novobiocin and neomycin; but two strains appear to be resistant to all, including these three, and several reports indicate resistance to all the common broad-spectrum antibiotics.

It is to be regretted that in none of the 337 cases was phage typing available; but in the Australia-wide series in course of preparation at the moment, nasal swabs have been taken in some thousands of consecutive cases of soft-tissue infection, with lesion swabs from all cases in which pus presented, and coagulase-sensitivity tests, phage typing and culture and sensitivity tests have been carried out on both lesions and nasal swabs. This should indicate the present status of drug therapy of the *S. aureus* with a great degree of certainty.

Summary.

1. A report is presented showing the incidence of penicillin-resistant staphylococci in 337 cases examined in general practice.

2. The material is "selected", in that sensitivity was examined in a number of cases only because of apparent clinical penicillin resistance.

3. The over-all penicillin sensitivity of the "general practice" staphylococcus in the series was 23·4%.

4. A comparison is made with a series of "hospital" staphylococci in which the penicillin sensitivity was 25·6%.

5. By way of further comparison in a series of consecutive unselected untreated soft-tissue infections, the incidence of penicillin sensitivity was 39·8%.

6. Observations are made on the clinical significance of these findings.

Acknowledgements.

My grateful thanks are due to the 26 members of the N.S.W. Faculty, who were kind enough to provide from one to 53 reports from which this series was compiled.

ISO-IMMUNIZATION IN A MOTHER WHICH DEMONSTRATES THE "NEW" Rh BLOOD ANTIGEN G (rh^G) AND ANTI-G (rh^G)

By RACHEL JAKOBOWICZ and R. T. SIMMONS,

The Red Cross Blood Transfusion Service (Victorian Division), and the Commonwealth Serum Laboratories, Melbourne.

ALLEN AND TIPPETT (1958) described a new Rh antigen discovered on the red cells of a woman named Crosby, which reacted with all anti-CD (Rh_o') sera, but not with specific anti-C (rh'), anti-D (Rh_o) or anti-E (rh") sera. As this Crosby antigen did not possess any individual "C-ness" or "D-ness", only a "CD-ness" combined, its discoverers suggested a new symbol for it—G (rh^G). The corresponding antibody would be anti-G (rh^G), and the gene r^G.

Absorption and elution tests showed that, although cells of pure G (rh^G) type are extremely rare, all red cells which have C (rh') or D (Rh_o) antigens also carry the factor G, and most sera which apparently contain anti-CD (Rh_o') consist of either anti-D (Rh_o) plus anti-G (rh^G), or anti-D (Rh_o) plus anti-G (rh^G) plus anti-C (rh').

This new factor G explains two paradoxes in blood group serology: (i) Exposure to the C (rh') antigen very rarely leads to the development of anti-C antibody (rh') in C– D+ E+ (Rh_o) individuals, while on the other hand anti-CD (Rh_o') is formed relatively frequently in C– D– E– (Rh-negative) persons sensitized with C+ D+ E– (Rh_1) blood. According to Allen and Tippett, the latter are examples of G, or D plus G sensitization, possible only in cde (Rh-negative) or cdE (rh") persons, as they are, generally speaking, the only ones whose red cells lack the G antigen. (ii) The G factor also explains why occasionally an Rh-negative (cde) woman with a C– D+ E+ (Rh_2) husband will produce antibodies of a CD (Rh_o') specificity, without using an extramarital relationship as a possible explanation for this serological phenomenon. In such cases we are dealing with a G sensitization, the G antigen being present with the husband's D (Rh_o) factor, the antibody produced consisting of anti-D (Rh_o) plus anti-G (rh^G).

This paper describes, as far as we know, the first case reported of G sensitization produced by the G factor present in Cde (rh') cells.

Report of a Case.

Mrs. W., Rh-negative, pregnant for the fourth time, had one living child, aged 14 years. A second pregnancy, 11 years previously, resulted in the birth of a stillborn child after eight months' gestation. Nine years previously she had had another stillborn child, prematurely born after seven months. She had never received any blood either by transfusion or by intramuscular injection. She was now pregnant again, and a sample of her blood was sent for investigation by Dr. Mary Meredith of Melbourne, because of an apparent discrepancy in the Rh antibody produced by Mrs. W., and the Rh antigen present on her husband's red cells.

Results of Tests.

In preliminary tests Mr. W.'s cells reacted as rh'rh (Cde/cde). More extensive tests, involving the use of three pools and 18 selected individual samples of incomplete anti-Rh_o (D) antisera, and several batches of anti-globulin serum, proved that the husband's cells were rh'rh (Cde/cde), and that no Rh_o (D^u) variant was present. In addition, the cells were tested with 12 agglutinating anti-Rh_o (D), 12 agglutinating anti-rh' (C), 12 agglutinating anti-rh" (E) sera, and numerous anti-Rh_o' (CD) sera. At least two of the anti-rh' (C) sera were obtained from D-positive (Rh_o) women. No variations on the initial results were observed. The only living child possessed all blood groups identical with those of the father. The blood of two brothers and two sisters of Mr. W. was also fully grouped, but these results have not been included in Table I because they provide no additional information.

TABLE I.

Blood Groups of the W. Family.

Antisera.	Mr. W.	Mrs. W.	Son W.
A	–	–	–
B	–	–	–
A+B	–	–	–
A_1	–	–	–
Result	0	0	0
M	+	+	+
N	–	–	–
S	+	+	+
Result	MS	MS	MS
Rh_o (D)	–	–	–
rh' (C)	+	–	+
rh^w (C^w)	–	–	–
rh" (E)	–	–	–
hr' (c)	+	+	+
hr" (e)	+	+	+
Result	r'r	rr	r'r
P	+	+	+
Lu^a	–	–	–
K	–	–	–
Le^a	–	+	–
Fy^a	–	–	–
Jk^a	+	+	+
Wr^a	–	–	–

Mrs. W.'s serum contained an incomplete antibody, acting on cells containing the C (rh') antigen as well as on those containing the D (Rh_o) antigen either on its own as cDe (Rh_o) or in combination with E as cDE (Rh_2). It did not act on Rh-negative or cdE (rh") cells. The antibody could be demonstrated by the indirect Coombs and serum-albumin methods and by the use of papain-treated cells. When the serum was first tested, the antibody titre was 64 against Rh_1Rh_1 and her husband's rh'rh cells. Against Rh_2 cells the titre was 32. The difference between these two titres is within the range of experimental error.

Samples of Mrs. W.'s serum were absorbed with equal parts of a 50% red-cell suspension from her husband and from donors of types Rh_1Rh_1, Rh_2, Rh_o, rh' and rh. The results of the absorption are shown in Table II.

Absorption with her husband's red cells removed not only anti-C (rh'), but apparently also anti-D (Rh_o) from Mrs. W.'s serum. Her husband's cells behaved like Rh_1Rh_1

(CDe/CDe) cells. Absorption with cells lacking C, but containing the D antigen, apparently absorbed the D part of the antibody, leaving an agglutinin behind which reacted with all cells containing the C antigen, although the titre of this anti-C antibody was reduced.

After contact with Mrs. W.'s serum, the eluate from Mr. W.'s cells contained an antibody acting on his own cells as well as on Rh_1Rh_1, Rh_0, Rh_2 and rh'rh cells. It did not act on rh" or rh cells.

Mr. W.'s red cells did not absorb any anti-D from pure anti-D sera, nor could any be eluted from them after contact with such sera.

TABLE II.

Titrations of Mrs. W.'s Serum after Cell Absorptions.

Cells Used for Absorption.	Test Cells and Titres.[2]					
	rh'rh	Rh_1Rh_1	Rh_2	Rh_0	rh'	rh
rh'rh(C)[1]	0	0	0	0	0	0
Rh_1Rh_1(CD) ..	0	0	0	0	0	0
Rh_2(DE) ..	4	8	0	0	8	0
Rh_0(D)	4	8	0	0	8	0
rh'(C)	0	0	0	0	0	0
rh(c)	32	32	16	16	32	0

[1] The rh'rh cells used were those of the husband.
[2] The titres observed after absorption with Rh-negative (rh) cells are taken as standard values.

Discussion.

Agglutination, absorption and elution tests indicate that Mr. W.'s Rh type is rh'rh. The Rh antibody in his wife's serum seems to have anti-D as well as anti-C specificity, as it acts on Rh_0 and Rh_2 cells as well as on Rh_1 and rh' cells, being inactive only with Rh-negative and rh" cells.

There is no history of transfusions to explain this D-like antibody, nor was it caused by sensitization to an Rh_0 (D^u) variant, as no such variant could be demonstrated on Mr. W.'s red cells. The antigenic stimulus must, however, have been provided by her husband's red cells, as the antibody could be absorbed by and eluted from them, although they did not absorb the anti-D from several pure anti-D sera.

While her husand's cells and cells of types Rh_1 and rh' removed all Rh antibodies, Rh_0 and Rh_2 cells only removed the total of the apparent D antibody from Mrs. W.'s serum, leaving behind an antibody which still reacted on Rh_1 and rh' cells — that is, one of anti-C specificity, which after absorption was of lower titre than prior to it. Absorption tests carried out with the red cells of Mrs. W.'s son gave identical results with those of the husband. Mrs. W. has developed anti-C as an immune response to her husband's C antigen, and also a second antibody which, though of apparent D specificity, fulfils all the criteria of Allen and Tippett's anti-G. It can be absorbed by, and subsequently eluted from, all Rh-positive cells containing C and/or D antigens, and is not active on rh" or Rh-negative cells. Mr. W.'s red cells, like most D-positive and C-positive cells, contain the G factor as an integral part of the C agglutinogen, and this factor has led to the development of an anti-G (rh^G) antibody, imitating the presence of an anti-D (Rh_0).

Summary.

The serum of a pregnant woman, Mrs. W., apparently contains anti-C (rh') plus anti-D (Rh_0) antibodies. It is her fourth pregnancy, the previous three having resulted in the birth of one living and two premature stillborn children.

Her husband and her son were of type rh'rh (Cde/cde), and neither possessed an Rh_0 (D^u) variant. There was no history of previous immunization with the Rh_0 (D) antigen.

After absorption with her husband's or son's red cells, Mrs. W.'s serum no longer acted on red cells containing the C and/or D antigens.

Eluates obtained from Mr. W.'s red cells after contact with Mrs. W.'s serum reacted on all types of Rh cells with the exception of rh (cde/cde) and rh" (cdE/cde) cells.

Absorption with Rh_0 (cDe) or Rh_2 (cDE) cells removed all anti-D (Rh_0) specificity, but left some anti-C (rh') antibody behind.

As a serological result of pregnancies, Mrs. W.'s serum contains anti-C (rh') plus anti-G (rh^G) antibodies.

The antigenic stimulus was most likely provided by fœtal rh' (Cde) cells, with strongly antigenic C (rh') and G (rh^G) factors inherited from the father.

Acknowledgements.

We wish to thank Dr. Mary Meredith and Dr. Margaret Mackie of Melbourne for referring this patient to us, and Mr. and Mrs. W. for their whole-hearted cooperation.

Reference.

ALLEN, F. H., and TIPPETT, P. A. (1958), "A New Rh Blood Type which Reveals the Rh Antigen G", *Vox. Sang. (Basel)*, 3 (N.S.): 321.

Addendum.

Since this paper has been submitted for publication, Mrs. W. had her labour induced four weeks prematurely and was delivered of a female child, who became rapidly jaundiced and required two exchange transfusions.

The child's red cells were Group O and reacted as rh'rh(CDe/cde). They gave a strong direct positive Coombs reaction. Anti Rh_0(D) as well as anti rh'(C) could be eluted from the cord cells, and both types of antibodies could be demonstrated in the cord serum, the anti rh'(C) at a slightly higher titre than the anti Rh_0(D).

A NEW DRUG IN RELIEF OF ANGINA PECTORIS: A PRELIMINARY REPORT.[1]

By L. N. GOLLAN,
Launceston.

MEDICAL HISTORY is rich with the stories of new drugs which have been introduced for the treatment of diseases and then discarded as being unsuitable, only to be later remembered because of certain side effects. After further research they are found to be dramatically effective in the treatment of a condition far removed from that for which they were originally intended; this is an example of serendipity. Iproniazid ("Marsilid", Roche) is such a drug.

Iproniazid was introduced originally in 1951 for the treatment of tuberculosis, and one of its first trials was carried out at the Montifiore Hospital, Bronx, New York. Subscribers to "Life International" at that time may remember two pages of photographs in that publication which showed patients at the Montifiore Hospital sitting up in bed looking bright and cheerful, some singing, others dancing in the middle of the ward between the beds and all obviously emotionally elevated. This was an unexpected scene in any chest hospital at that time, for although streptomycin had been in use for two or three years the usual picture was still that of depression and hopelessness.

In 1957 both Kline (1958) and Crane (1956) reported to the American Psychiatric Society the results of a study of iproniazid on the depressed patient. Results were promising, and it was after that meeting that the drug began to be used widely for the treatment of depression. It is of interest to note that the drug benefits depression only and not anxiety, which in fact it may even accentuate.

It was noted during those trials that patients who also suffered with angina pectoris, after a short period, found that they were having much less pain or that

[1] Read at a clinical meeting at the Launceston General Hospital, September 11, 1958.

it had disappeared completely. A new avenue was thus opened to research.

Iproniazid is a derivative of isoniazid, and is available in tablets as iproniazid phosphate equivalent to 50 mg. of iproniazid. It has anti-tubercular properties very similar to those of isoniazid. It has a stimulating effect on appetite and weight-gain in some cases, and also has a marked elevating effect on mood. In addition, it is most effective in relieving angina pectoris, and it has been reported that in some cases blood pressure and blood-sugar levels have also been reduced.

It is possible that some of these effects may be due to the fact that iproniazid is a potent inhibiter of amine oxidases. Thus inhibition of monoamine oxidases (which break down serotinin) indirectly potentiates serotinin and probably accounts for the action of iproniazid on the nervous system. Reserpine, on the other hand, lowers the level of serotinin in the brain and thus is a tranquillizer. In addition, by inhibiting the specific amine oxidases, both adrenaline and noradrenaline may be protected from breakdown, and as both these substances produce dilatation of the coronary arteries and increased coronary flow, this is a possible explanation of the effectiveness of the drug in relieving angina pectoris. On the other hand, however, it may be brought about by acting directly on cardiac metabolic and enzymic processes and modifying their demands.

Therapeutically, therefore, it appears that iproniazid may be most effective for tuberculosis, both pulmonary and extrapulmonary, for depressive states (without anxiety) and for angina pectoris.

The side effects of iproniazid are similar to those of isoniazid, but are reported to be more severe and to occur more frequently and in particular are more likely to produce central nervous system reactions. Those reactions recognized are muscle tremor, constipation, difficulty in micturition, orthostatic hypotension, insomnia, headache, giddiness and peripheral neuritis, which is manifest first by tingling and parasthesia of the limbs and which later may be followed by weakness, paralysis of muscles and loss of deep reflexes. Psychotic episodes or even epileptic fits may be encountered occasionally, but usually only in patients who have had a previous history of epilepsy or a psychotic illness. The drug should not be used for patients suffering with liver damage as jaundice has been described as one of the rarer complications.

This series of cases on which I am giving a preliminary report is only small. The patients are drawn from my private practice and do not include all patients under treatment with iproniazid. It is a selected series, and numbers only 15. The period under observation ranges up to five months.

Patients were selected who suffered from relatively severe to very severe angina pectoris, unrelieved by any drug other than glyceryl trinitrate. These fell into two main groups: first those who for economic reasons found it essential to continue earning their own living in the only trade or occupation they knew; secondly those in the older age group, especially those who had retired, whose main complaint was that exercise tolerance was so greatly limited, because of the frequent and severe chest pain, that life was hardly worth living.

Grading of the degree of angina is difficult as it depends upon subjective symptoms only, and I do not think there is any way of accurately assessing the severity, such as by estimating the average number of trinitrin tablets taken each day over a period, for there is no constant factor day by day or week by week in any one patient.

All these patients under review had been given at some stage one or all of the following: pentaerythritol tetranitrate, triethanolamine trinitrate, aminophylline and the Rauwolfia preparations in addition to glyceryl trinitrate. I have found that, apart from the last, these drugs are disappointing in relieving angina pectoris of any degree of severity. Kalmanson in 1955 reported that pentaerythritol tetranitrate is not effective in any dosage in producing coronary dilatation and relieving angina pectoris. Rauwolfia I have found has never helped any patient with angina pectoris on whom it was tried.

Of these 15 patients 11 were males and four were females. Their ages ranged from 48 to 87 years, the average age being 63 years. Symptoms had been present before treatment was commenced from six months up to eight years and averaged four and half years.

Six patients had suffered one or more cardiac infarctions before treatment was commenced, and seven patients had the following associated diseases: silicosis with emphysema and congestive cardiac failure, one patient; chronic bronchitis, pulmonary emphysema and cardiac failure, one patient; diabetes mellitus, three patients; arteriosclerosis and congestive cardiac failure, one patient; arteriosclerosis with hemiplegia, one patient.

Two patients, when treatment was commenced, were in a condition of cardiac ischæmia with constant anginal pain. One was admitted to hospital at the same time that iproniazid was started, and commenced anticoagulant therapy. The second one refused to be treated in hospital and was treated at home with iproniazid alone.

Treatment was commenced initially with 50 mg. three times daily and later reduced as thought necessary, although a number of patients are still on the original dose. All other drugs used in the treatment of angina pectoris except glyceryl trinitrate were suspended. Patients with heart failure were continued on digitalis and diuretics, and those with diabetes continued their usual anti-diabetic treatment.

The length of time before the first signs of improvement occurred showed considerable variation, although the average time did not differ very much from published results. The maximum improvement does not occur rapidly after first signs of improvement are noted, but rather there is a steady improvement with lessening of pain and improvement in exercise tolerance. with a corresponding reduction in the number of glyceryl trinitrate tablets needed. In one case lessening of pain was noted within three days, but over the whole series first signs of reduction of pain were not noted until eight or nine days had elapsed, whilst the maximum relief was not reached until two weeks after the drug was started. One patient did not obtain maximum relief for 28 days and did not show any improvement until 14 days after treatment had commenced.

As regards the two cases of cardiac ischæmia, the patient who was admitted to hospital and started on anticoagulant therapy as well as iproniazid was completely pain-free in three days. Later, after his discharge from hospital, his iproniazid was inadvertently ceased, and within three days his pain had returned with increasing severity, but this cleared again within five days of recommencing therapy. The second patient had started to improve within four days, and was pain-free by the fifteenth day, but on the thirteenth day she had pain of great severity, which lasted for 12 hours, and it was thought she had suffered a cardiac infarction. At present she has no angina and requires no more glyceryl trinitrate.

Cesarman (1957) in his series found that the first response occurred about the third day and total response by the twelfth day.

Cossio (1957), on the other hand, reports that he found the first relief of pain to occur between the third and the seventh day and the maximum effect by the second and third week.

Only one patient in this series received no benefit from the drug. In one case treatment, although effective, had to be ceased because of the side effects produced. The remaining 13 received moderate to complete relief, and in them all there was a concurrent elevation of mood and a feeling of well-being. Exercise tolerance was correspondingly improved.

Of the 14 patients who received benefit from the drug, the response was as follows: complete relief of pain, eight patients; considerable relief of pain with only occasional discomfort in the chest not requiring glyceryl trinitrate, three patients; chest pain still produced by

exertion, but much less severe, and the number of glyceryl trinitrate tablets used considerably reduced, three patients.

As mentioned earlier, it has been reported that the drug may produce a fall in blood pressure. This was noted in four cases in which there was previous hypertension. The systolic fall averaged 35 mm. of mercury and the diastolic 15 mm. of mercury. One patient was having chlorothiazide for congestive cardiac failure, but no other hypotensive drug. Two other patients with moderate hypertension showed no alteration in their blood pressure, and the remaining nine normotensive patients also showed no alteration in their blood pressure readings. All readings were taken with the patient in the recumbent position, but Harnes (1958), on a series of 17 cases, found postural hypotension in 15 of them.

The majority of patients in this series had electrocardiographic tracings taken before and after treatment. There were some minor changes noted in some of the tracings, but these were not constant, so it is impossible to draw any conclusion in such a small series as this.

The effect of iproniazid on the prothrombin index was also investigated, and the conclusions drawn were that this is not in any way affected. Those patients who were having anticoagulant therapy when iproniazid was commenced required no adjustment of the dosage of the anticoagulant drug to keep the prothrombin index at a steady level. The remaining patients in this series all showed a normal prothrombin index after they had been taking the drug for some time.

As yet facilities are not available in this city for the estimation of transaminase levels, so the effects of iproniazid on serum transaminase levels could not be investigated.

However, Dr. J. Marks, of Roche Ltd., London, advises that work done in this field shows that 30% of patients taking the drug have a raised transaminase level, which subsequently falls to normal when the drug is withheld. This, however, does not appear to be related to changes in the heart muscle, as it occurs also during the treatment of depressive states in otherwise normal patients, and at the moment it is not possible to express any views on the significance of this observation.

The following side effects were encountered by seven patients: giddiness, four patients; depression of sexual function, one patient; peripheral neuritis, one patient; precipitation of asthmatic attacks, one patient.

Of these, giddiness was severe in two cases and in both instances produced such a degree of intermittent ataxia that falls with subsequent soft tissue injury occurred. The peripheral neuritis (manifested by numbness and tingling and later by a severe pain in one leg) cleared quickly after pyridoxine in doses of 50 mg. three times a day was administered. This was ceased after two weeks, but the pain recurred within two days, so the dose was resumed with subsequent rapid relief of symptoms again.

One patient who has not been worried with asthma for several years developed a severe attack each time the drug was administered. The attack cleared about three days after it was ceased. Although she had satisfactory relief from her angina, after three attacks of asthma she refused to take the drug any more.

Three patients in the series died, three, four and eight weeks respectively after they commenced treatment. The first patient had severe giddiness whilst the drug was being administered and received no relief from his angina pectoris. He died suddenly after a spontaneous pneumothorax. He suffered from silicosis and emphysema, and shortly before the drug was administered had an episode of severe congestive cardiac failure. The second patient, who had complete relief from pain and who had been on anticoagulant therapy for some time, died suddenly of her sixth cardiac infarction after having had the fifth fourteen days previously. The third patient, who also had complete relief from symptoms and who also had been on anticoagulant therapy, died of his second cardiac infarction nine months after his first.

Summary.

The effects of iproniazid were observed in a selected series of 15 cases over a period of five months. These patients suffered with moderate to severe angina pectoris and had received no benefit from other drugs.

All but one patient experienced some degree of relief. Eight obtained complete relief and did not require to take any glyceryl trinitrate. Six received moderately good relief.

One patient left off the drug because of the side effects produced.

All but two experienced some elevation of mood.

The blood pressures of four patients with hypertension were significantly reduced.

Electrocardiographic studies revealed no changes of any significance.

The prothrombin level does not appear to be altered. In 30% of cases the transaminase level is elevated, but this does not appear to be connected with damage of cardiac muscle.

Optimum dosage appears to lie between 100 and 150 mg. per day. Below 75 mg. daily the drug is ineffective.

In spite of some unpleasant side effects, the drug appears to be so effective in the relief of pain of angina pectoris that it will almost certainly become widely used for this condition.

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Reports of Cases.

LEUCOTRICHIA TOTALIS FROM CHLOROQUINE.

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LEUCOTRICHIA can be congenital or acquired, physiological or pathological, and generalized or partial.

It is the purpose of this communication to report the occurrence of generalized leucotrichia in a young man who previously had dark brown hair, and who was undergoing chloroquine therapy at the time.

Clinical Record.

The patient, a man, aged 20 years, who had dark brown hair, was diagnosed as suffering from a light sensitivity eruption, which involved the exposed areas of his arms and face.

In September, 1957, tablets of chloroquine base, 150 mg., were prescribed, one to be taken twice daily after meals. After two months of this treatment, the rash had improved considerably, but as progress had become slower, the dose of chloroquine base was increased to 150 mg. three times each day.

The patient was examined again in January, 1958, after having completed four months' treatment. It was found that his rash had nearly cleared, but that during the previous week all the hair of his scalp, eyebrows, eyelashes, pubic region and limbs had become bleached to an off-white colour. The chloroquine therapy was stopped immediately and six weeks later his hair had begun to show signs of repigmentation.

Discussion.

The significant points in this case are that the patient had dark brown hair, he was undergoing chloroquine therapy, the depigmentation of his hair was generalized and complete, and at no time were any other signs evident of toxic reaction to chloroquine.

In 1948, Alving *et alii* first reported that bleaching of the hair had occurred in all blond subjects taking chloroquine. During his investigation, 0·3 gramme of chloroquine base was given daily for 77 days, and then 0·5 gramme weekly for up to one year. Christiansen and Brodthagen (1956) also described the depigmentation of all scalp hair in two blond patients taking chloroquine, and Christiansen (1957) mentions this occurrence in a further three blond patients who were receiving between 150 mg. and 450 mg. of chloroquine base daily. Fuld (1956) also reported two patients on chloroquine therapy whose scalp, hair and eyebrows had changed from dark blond to very fair in colour, and who were very pleased with their apparent rejuvenation.

As far as can be ascertained, neither the depigmentation of dark brown hair nor the involvement of all the hair of the body has previously been reported in a patient undergoing chloroquine therapy.

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AN UNUSUAL COMPLICATION RESULTING FROM AMPHETAMINE SULPHATE ("BENZEDRINE"): A CASE REPORT.

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AMPHETAMINE SULPHATE was first introduced into clinical medicine by Prinzmetal and Bloomberg (1935), who discovered the usefulness of this drug in the treatment of narcolepsy. The euphoric effects of "Benzedrine" were first noted by Peoples and Guttman (1936). Guttman and Sargant (1937) reported the psychological effects of the drug, namely an increase in verbal and motor activity, elevation of the mood and prevention of drowsiness and sleep. The drug is also used to combat apathy, fatigue, hunger and depression. Transient psychotic episodes of a delirious type and dysmnesic syndromes are occasionally seen with overdosage of "Benzedrine".

The present report will be of interest since an exhaustive search of the comparatively voluminous literature concerning this drug fails to reveal that severe muscular fibrillation and fasciculation simulating motor neurone disease have ever occurred with overdosage of amphetamine sulphate.

Clinical Record.

The patient, a law student, aged 27 years, was found to be suffering from "irrational behaviour". On admission to hospital he was agitated and irritable, pacing up and down his room. He refused to eat and was very suspicious. He was frightened and had ideas of reference. This trouble was of two weeks' duration. His previous history showed that he was a quiet and serious man of good personality. There was nothing significant in his family history.

On examination his cerebro-vascular system showed no abnormalities. His blood pressure was 128/80 mm. of mercury. His chest was normal. Findings in the central nervous system were as follows. His pupils and fundi were normal, and tendon jerks were brisk. He had severe muscular fibrillation, and on percussion of any muscle there was a tremendous spasm and fasciculation of the segment percussed, which was sustained for two to three seconds; this was very similar to motor neurone disease. There was no muscle wasting. His jaw jerk was brisk. The Wassermann and Kahn tests gave negative results. Analysis of the urine showed no abnormalities.

In view of the patient's age and short history, or rather the acute onset of psychological symptoms as well as the lack of muscle wasting, a diagnosis of amyotrophic lateral sclerosis was excluded. It was decided to keep the patient under observation for a few days, to administer sedatives and to treat him as for a toxi-confusional state. In about 48 hours the patient became less irritable and much more accessible, and he told us that he was studying for his final law examination; as he could not keep awake he took "Benzedrine" tablets, at first 10 mg. a day, but nearer the examination some 600 mg. daily for a period of two and a half weeks. After 12 days in hospital the patient fully recovered and was discharged. Although his severe muscular fibrillation disappeared, slight twitchings were present six months after his discharge, together with slight paræsthesia.

Comment.

It is well known that great tolerance may be established with this drug, and Knapp (1952) has reported that 10 out of 13 of his patients reached a daily dose of 100 to 700 mg. without showing any physical disability.

While the central action of "Benzedrine" has been abundantly demonstrated, the drug has never been known to stimulate both the motor area of the cortex and possibly the anterior horn cells of the spinal cord, to produce severe muscular spasm and fasciculation.

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[1] This case was reported while Dr. Fischer was Medical Superintendent at Balderton Hospital, Newark, Nottingham, England.

INTESTINAL OBSTRUCTION DUE TO IMPACTION OF ORANGE PITH AFTER PARTIAL GASTRECTOMY.

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A PAPER by Spurzem and Desser (1957), an abstract of which appeared in the issue of this Journal of May 3, 1958, drew attention to 12 recorded cases of small-bowel obstruction following partial gastrectomy due to the impaction of phytobezoars. They reported two more cases. Two facts were emphasized: firstly, that most of the phytobezoars were composed of masses of citrus fruit fibre, and secondly, that the gastrectomy was always of the Pólya type with a gastro-jejunostomy. Their conclusion was that this type of gastric resection must be considered to be a predisposing factor to intestinal obstruction by foodstuffs.

Small-bowel obstruction under these circumstances is probably more frequent than Spurzem and Desser's report indicates, and it is with this in mind that the following case is reported.

Clinical Record.

A male patient, aged 71 years, had a Pólya gastrectomy performed on February 16, 1957, because of hæmorrhage from a recurrent duodenal ulcer. He was well until

readmitted to the Royal Melbourne Hospital on October 31, 1957, with severe central abdominal colicky pain and vomiting. These symptoms had become progressively worse over a period of 24 hours after a sudden onset. He had not opened his bowels or passed any flatus during this time.

On examination of the patient, his temperature was 99·2° F., his pulse rate was 62 per minute and his blood pressure was 200/100 mm. of mercury. His tongue was coated and dry, but his breath was not offensive. His abdomen was slightly distended centrally and tender all over, but to the left of the umbilicus there was added rigidity with release tenderness. A provisional diagnosis of small-bowel obstruction due to adhesions was made, and the obstruction was confirmed by a plain X-ray film of the abdomen with the patient upright; this showed multiple distended loops of small bowel with fluid levels. Gas was almost absent from the colon and rectum.

An intravenous infusion of normal saline was commenced, and the stomach was aspirated through an indwelling Ryle's tube. Under general anæsthesia a right mid-paramedian incision was made. No adhesions to the original mid-line abdominal incision were found. Collapsed small bowel was traced proximally to the site of obstruction in the lower part of the ileum. Here was a firm, cigar-shaped mass of matted fibre within the lumen, above which the bowel was grossly dilated. An attempt was made to break up the mass from outside and to move it down to and through the ileo-caecal valve. This proved impossible, and so the ileum was opened longitudinally and the mass was removed. The opening in the bowel was closed transversely. Convalescence was uneventful.

The mass was made up of tightly wrapped sheets of unchewed orange fibre and pith. Subsequently the patient said that his practice had been to eat an orange a day after his gastrectomy.

Conclusion.

Small-bowel obstruction is not a frequent complication of partial gastrectomy, but it would seem that foodstuff masses may account for quite a number of the cases that do occur. It would probably be wise to warn patients who have had Pólya gastrectomies and gastroenterostomies to masticate vegetable fibres very thoroughly.

Acknowledgement.

I would like to thank Mr. Howard H. Eddey for permission to report this case.

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Reviews.

Heredity Counseling. Edited by Helen G. Hammons; 1959. New York: A Hoeber-Harper Book. 8" x 5¼", pp. 128. Price: $4.00.

IN this Journal on June 28, 1956, there appeared a favourable review of an American book "Counseling in Medical Genetics", by Sheldon C. Reed. The same author, now in collaboration with 16 colleagues, presents a similar message, but in fuller detail. Each contributor gives a brief description from a separate angle of one particular aspect of the problem. One chapter, "Genetics and Dentistry", contains something quite new, and is the only one in which the characteristic terminology of genetical writing appears. The book is divided into two fairly equal parts; the first is "Genetics in Medical Practice", the second is "Heredity Counseling". Medical genetics is now to be regarded as an important branch of public health administration, and should be understood by the general practitioner, for, when advice is sought with regard to the desirability of having children or of adoption, it is the family doctor who will be consulted and not the genetic specialist. An admirable sanity and restraint pervade the whole book. The reader is cautioned about the many gaps in our knowledge, and a useful list of "don'ts" is given. According to one author, "heredity counseling is in the next few decades going to steer into stormy water". We are told that there are 40 separate types of mental retardation, and knowledge of their transmissibility is fragmentary. It is estimated that each of us carries at least eight rare hidden genes, and just what is going to happen as the result of casual mating is hard to determine. The general practitioner, as well as the obstetrician, will be interested in one of the conclusions—namely, the heritability of a tendency to hypertensive toxæmia of pregnancy. As in Sheldon Reed's earlier book, the practitioner is advised not to give a dogmatic "yes" or "no" to a query regarding pregnancy, but to present the inquirer with a number expressing approximately the risks likely to be encountered.

Staphylococcus Pyogenes and its Relation to Disease. By Stephen D. Elek, M.D., D.Sc., Ph.D., D.P.H.; 1958. Edinburgh and London: E. and S. Livingstone, Limited. 9½" x 5½", pp. 776, with illustrations. Price: 84s. (English).

IN recent years, the staphylococci have attracted more attention than most other pathogenic bacteria; this has been chiefly due to the emergence of antibiotic-resistant strains and their implication in epidemics of hospital infection. At the same time, the increasing clinical importance of infections with these cocci has underlined our ignorance concerning the more fundamental problems of their pathogenesis.

The present book is designed for the laboratory worker rather than for the clinician, and in it Professor Elek has attempted to summarize our present knowledge. This has involved the compilation of a bibliography containing approximately 5000 references, which will prove of great value to all interested in this ubiquitous parasite.

The staphylococcus is discussed in its various biological aspects. Chapters are concerned with morphology, taxonomy, metabolism, antigenic structure, phage typing, genetics and natural habitats. The effects of physical agents, of antiseptics and chemotherapeutic agents and of antibiotics are also dealt with *in extenso*. In the chapters on virulence and on host resistance the mechanisms of pathogenesis are fully discussed, including the vexed questions of how initial lesions are produced and whether strains of enhanced virulence exist. The author considers that hypersensitivity plays no part in staphylococcal disease, a view which will not be accepted by all bacteriologists.

This book may be regarded as a valuable addition to microbiological literature, and as a jumping-off place for further research.

Nutrition and Atherosclerosis. By Louis N. Katz, M.D., Jeremiah Stamler, M.D., and Ruth Pick, M.D.; 1958. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9" x 5½", pp. 146, with 66 illustrations. Price: 55s.

A GREAT deal has been written over the past few years in attempts to explain the causation of atherosclerosis. At the present the stress is on possible nutritional causes. The time is ripe for a balanced and critical review of the ideas about causation which have been published. Such a review is given adequately in this book. The authors present a nutritional-metabolic cholesterol-lipid-lipoprotein theory of atherogenesis. The atherogenic alterations in metabolism are frequently brought about by the life-span pattern of diet—a diet excessive in calories—empty calories, that is, from processed food high in energy value but low in essential nutrients (minerals, vitamins, essential amino acids and essential fatty acids)—and inadequate in certain foodstuffs. They discuss the evidence under several headings. The first is "Epidemiologic Findings"—that is, the diet in different countries and the possible relation of this to the incidence of atherosclerosis. The second heading is "Clinical-Pathological Findings"—the changes in the blood lipids and cholesterol in atherosclerosis and the relation of these to diet. The third is "Animal-Experimental Findings"—the pathological changes produced in the blood vessels of laboratory animals after certain diets. Hormonal and other endogenous factors are also discussed. A complete account is given of the epidemiological findings. The effect on serum cholesterol following substitution of vegetable fat for animal fat is discussed fully and in a well-balanced way. The authors also consider the hormonal factors and other endogenous factors which may be concerned in atherosclerosis, particularly the sex hormones and the relative infrequency of atherosclerosis in women prior to the menopause in contrast with men under 40 years of age. In this discussion they stress that they attribute a key—but not exclusive—role to diet, but atherosclerosis is not simply a dietary disease. The whole

discussion on the causation of atherosclerosis is very detailed, very critical and very satisfying. Finally, a good summing up is given of the possible approaches to prophylaxis and therapy. A few pages of specific recommendations, both for prophylaxis and for treatment, are given. These are safe, simple and reasonable and can be followed by anyone—even a gourmet—without any hardship and almost certainly with profit. To indicate the field covered by the authors the bibliography cites 787 references, and yet the text of the book covers less than 100 pages. It is a book to be thoroughly recommended to all medical men.

An Atlas of Surgery. By F. Wilson Harlow, M.B., B.S. (Durham), F.R.C.S. (England), with a foreword by Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., D.Sc., F.R.C.S.; 1958. London: William Heinemann (Medical Books), Limited. 13½" × 8½", pp. 320, with 1292 illustrations. Price: 50s. (English).

THIS new atlas is designed, the author tells us in his preface, as a "pictorial aide-mémoire of common and important surgical facts and procedures". For the medical student it is introductory to clinical surgery and "a supplement to, not a substitute for, the standard text books". For sisters and nurses it is "an aid to surgical training and the understanding of the reasons underlying surgical practice".

The author attempts to cover a very wide field in eight sections on abdominal surgery, urology, gynæcology (including some obstetrics), general surgery, special surgery (throat, nose and ear, thoracic and neurological surgery), orthopædics, management of operations and surgical pathology. With such a scope many themes must be dealt with very inadequately, and are better handled pictorially in standard textbooks. Some sections, such as that on labour, and many diagrams could be omitted without loss, to the beneficial expansion of others, such as that on acute appendicitis, without undue enlargement of the volume. A number of inaccuracies in both text and diagrams will doubtless be corrected in subsequent editions. For example, the neck of an inguinal hernial sac is said to be medial to the pubic spine, and thyroid hormone is said to cause exophthalmos. Black and white photographs frequently leave much to be desired, and it is also hoped that some illustrations will be replaced by clearer ones. Figures 13, 118, 209 and 495 contrast with some excellent pictures.

These criticisms, however, should not be allowed to detract unduly from the general standard of this book and the commendable aims of its author. The foreword by Sir Cecil Wakeley commends the book wholeheartedly, and rightly stresses the value of the pictorial method in teaching and learning. In the library of a nursing training school the book should fulfil its aims most admirably. For the medical student, its value in its present form is not so clear, but, improved, it could be a useful companion to standard surgical texts, much as an atlas serves as an aid to the student of a text of anatomy.

***A Synopsis of Hygiene* (Jameson and Parkinson).** By Llywelyn Roberts, M.D., M.R.C.P., D.P.H., assisted by Kathleen M. Shaw, M.B.E.; Eleventh Edition; 1958. London: J. and A. Churchill, Limited. 9¼" × 6", pp. 702, with 22 illustrations. Price 60s. (English).

TEXTBOOKS on hygiene and public health written and published in Britain have but a limited market in Australia, but in the absence of an Australian textbook on these subjects they are necessary to medical officers of health and students for the diploma of public health as works of reference. Among them one of the best known is "Jameson and Parkinson", and to those who keep a copy on their shelves the appearance of an eleventh edition of "A Synopsis of Hygiene", now edited by Llewelyn Roberts and Kathleen Shaw, will be welcome. Although as in the previous edition the general arrangement adopted by its original authors has been preserved, to offset the additional material which has had to be incorporated the entire format of the volume has been changed and reset in a larger page.

Almost one-third of the volume deals with public health law and administration, and with hospital and other health services and agencies in England and Wales only. Little of this portion of the work is of interest to Australian readers. Of the remainder, there has been but little change in the four sections which are devoted to environmental sanitation. In view of the growing anxiety about the possibility of radioactive contamination of air and water, it is rather surprising that more space has not been given to this aspect of communal hygiene.

The most useful part of the book is that composed of the remaining three sections, which comprise at least half of the volume. Section II, headed "Infections and Other Conditions of Epidemiological Interest", could well have been divided. It deals not only with the prevention and control of infectious diseases, occupation and health, non-infectious diseases and disabilities, but also with rehabilitation, mental illness, animals and insects in relation to human health and other matters. Section IV is devoted to the care of mother and child, and Section V to nutrition and food. These are all readable and packed with useful information, even if the statistical tables and diagrams, of which there are many, apply only to England and Wales. Illustrations are few, and restricted to the section on building construction. The indexing is good.

A notable feature is the absence of irritating footnotes and a bibliography. In their place, at the end of each paragraph are given references to the literature on the subjects dealt with in that paragraph, a commendable practice which enhances the value of the volume as a work of reference.

Autopsy Diagnosis and Technic. By Otto Saphir, M.D.; Fourth Edition; 1958. New York: Paul B. Hoeber, Incorporated. 7½" × 5", pp. 576, with 78 illustrations. Price: $8.50.

THE fourth edition of this work is a handy, practical manual for use in the autopsy room. It is what it claims to be, a handbook giving a diagnostic outline of the gross lesions commonly encountered at autopsy. It does not lay stress on histology, nor does it deal in particular with medico-legal autopsies.

The method of autopsy technique described is the one that has been found most useful in the hands of the author. Removal of the organs *en masse* is favoured. At the beginning of each section, the procedure for removal of the organs and their individual examination is described. The text is illustrated with appropriate diagrams showing technical procedure and illustrating various anatomical aspects. Tables are included giving the main differential diagnostic points in diseases of the kidney, thyroid, liver, spleen, etc.

Three new chapters have been included in this edition. There is a valuable short historical account of the autopsy. A chapter has been introduced on bodies treated with radioactive isotopes, and the precautionary methods to be adopted are set out. The collection and storage of autopsy material for the "tissue bank" has also been discussed; increasing use is being made of this material for the benefit of the living.

There is a wealth of valuable, practical information in this book, which is well set out and easy to read, and would be useful for reference in every post-mortem room.

Cyclopropane Anesthesia. By Benjamin Howard Robbins, B.A., M.S., M.D.; Second Edition; 1958. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 8½" × 5½", pp. 308, with 74 illustrations. Price: 90s.

THE dictionary by Gould states that a monograph is a treatise on a single subject; yet this second edition of "Cyclopropane Anesthesia" by Robbins has included in it a full chapter on relaxing agents. Of course, cyclopropane was the anæsthetic agent used by Griffith when curare was first clinically administered in anæsthetic practice; but there appears to be no reason why the history and pharmacology of all the relaxants should be discussed. Although the author is known for other published work on cyclopropane, the first edition of this book appears to be unknown in this country. Perhaps its time of publication (1940) restricted its distribution.

The book consists of 12 chapters profusely illustrated with graphs, tables, electrocardiograms and kymographs. Herein may be found in detail all the known properties of cyclopropane. The preface informs us that the reasons for the publication of this second edition (such a long time after the first) are, firstly, that several leading anæsthesiologists have stated that the agent is almost the ideal one and should be used more widely, and secondly, that in the United States the production and use of the gas have doubled in the past five years. Both statements need critical examination. To support the author's thesis, such authorities as Neff are quoted. Neff's opinion and all but two of 18 other opinions are quoted from papers published prior to Neff's work of 1942 on nitrous oxide with pethidine supplementation. Further, it is well known that certain techniques are practised in certain centres almost to the exclusion of all others. The second reason, concerning increased production, also applies in this country. The distributors have informed us that the sale of this agent has increased by some 40% in the last three

years. However, at two of our teaching hospitals the incidence of administration has increased only by 0·3% and 1·2% during this time. This fortifies our opinion that probably in America, as here, more anæsthetists have become qualified to use the agent, not that the agent is being used any more widely by individual anæsthetists, except the few who choose this agent almost to the exclusion of all others.

A more critical assessment is made by the author in the chapter on indications for the use of the agent; but even here not all will agree with him. The anæsthetic has several disadvantages, the two most important of which have not been overcome. These are its extreme explosiveness throughout its anæsthetic range and the arrhythmias associated with its use. The author has an original contribution to offer for the control of these latter disturbing phenomena, but as yet this work is unconfirmed. There is no doubt that arrhythmias occur with any general anæsthetic. There is also no doubt that the incidence is greater with cyclopropane. For this reason and others not detailed in this review, the use of this agent must be restricted to specialists in the art. The book therefore, will have a limited appeal.

There is a mass of detail of experimental work on animals. This detracts from the value of the book for general reading. However, to offset this, there is a short summary concluding each chapter. For easy reading this is ideal, but in this instance becomes very expensive, as this book of some 286 pages will retail for 99s. Further, the relevant information can be obtained from any good standard textbook on anæsthetics. Therefore, the publication seems to be destined for libraries as a reference book. The bibliography must be the most complete one to date on the subject matter, and for convenience is arranged in alphabetical order.

The book is from the house of the Williams and Wilkins Company and, as far as production is concerned, lives up to their motto of *"Sans tache"*.

Diseases of Women. By Ten Teachers, under the direction of Frederick W. Roques, C.B.E., M.D., M.Chir., F.R.C.S., F.R.C.O.G., edited by Frederick W. Roques, John Beattie and Joseph Wrigley; Tenth Edition; 1959. London: Edward Arnold (Publishers), Limited. 8¼" × 5½", pp. 576, with 209 illustrations. Price: 36s. (English).

For forty years, "Diseases of Women" by "Ten Teachers" has represented the standard gynæcological teachings for English students. This tenth edition has been slightly enlarged, and in many places rewritten. Vaginal cytology has been included for the first time, and the chapters on genital prolapse, tuberculous salpingitis and gynæcological operations are almost entirely new. Gynæcological anatomy and physiology are dealt with briefly but adequately, and there is a good chapter on malformations. Backache as a symptom is treated as a separate entity, and it is pleasing to see its orthopædic aspects stressed.

Reading the section on sterility, the student gathers that most treatments are of no avail—altogether too pessimistic an approach, and one that is at variance with world statistics.

In the discussion of carcinoma of the uterus, modern cytological methods are described, but no mention is made of the colposcope to visualize the suspicious cervix. Papanicolaou smear examinations are made to appear too accurate and easy, and it should be stressed to the student that their value varies directly with the experience of a trained pathologist.

Many practitioners, as well as students, would do well to read the excellent chapter on neurasthenia and neurosis in relation to pelvic disorders. Psychosomatic manifestations seem particularly prone to occur in gynæcological practice, and if the whole woman, mind as well as body, received due consideration, a great number of unnecessary abdominal sections would be avoided.

The book concludes with a very short and sketchy chapter on gynæcological operations. Hospital administrators in this country would view with a jaundiced eye the suggestion on page 497 that "in the case of minor operations, such as dilatation and curettage . . . the patient may leave the hospital on the fifth or sixth day".

This textbook was produced primarily for the use of medical students, and for this purpose it can be well recommended. But it is, as well, an excellent and sound reference book for any general practitioner who practises gynæcology. It is nicely set up and printed, but would be improved with rather more illustrations, those on operative techniques being particularly poor.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Bronchography", by C. Dijkstra, M.D.; 1959. Oxford: Blackwell Scientific Publications. 9½" × 6½", pp. 158, with 106 illustrations. Price: 45s. (English).

Written for the general medical reader rather than the specialist.

"A Manual of Psychiatry", by K. R. Stallworthy, M.B., Ch.B.; Fourth edition; 1959. Christchurch: N. M. Peryer Limited. 7¼" × 4½", pp. 365. Price: 30s. (New Zealand).

Written for the elementary student.

"Infant Mortality in India, 1901-55: A Matter of Life and Death", by S. Chandrasekhar, with a Foreword by Professor Philip M. Hauser; 1959. London: George Allen & Unwin, Limited. 8½" × 5", pp. 176. Price: 20s. (English).

The result of a research inquiry carried out by the author as a Nuffield Foundation Fellow in the London School of Economics.

"The Mast Cells", by James F. Riley, M.B., Ch.B. (Hons.), M.D., Ph.D., D.M.R.T., F.R.C.S.E., with a foreword by Sir Henry Dale, O.M., G.B.E., F.R.C.P., F.R.S.; 1959. Edinburgh and London: E. & S. Livingstone Limited. 9½" × 6½", pp. 194, with 65 illustrations. Price: 30s. (English).

The book is in two parts: first, a review of the literature; second, the author's thesis, "Functions of the Tissue Mast Cells", accepted by the University of St. Andrews for the degree of Doctor of Philosophy.

"Total Surgical Management", by J. D. Hardy, M.S., M.D., F.A.C.S.; First Edition; 1959. New York and London: Grune & Stratton. 9" × 6", pp. 298, with illustrations. Price: $9.50.

An attempt to give a comprehensive account of the subject.

"Clinical Obstetrics and Gynecology", Volume 2, Number 1: March, 1959. "Menstrual Disorders", edited by C. Frederic Fluhmann, M.D.; "Spontaneous Abortion", edited by David N. Danforth, M.D. New York: Paul B. Hoeber, Inc. 9½" × 5½", pp. 252, with illustrations. Price: $18.00 per year.

A quarterly publication.

"Radiation Biology and Cancer: A Collection of Papers Presented at the Twelfth Annual Symposium on Fundamental Cancer Research, 1958", published for the University of Texas M. D. Anderson Hospital and Tumor Institute; First Edition; 1959. Austin: University of Texas Press. 9" × 5½", pp. 493, with illustrations. Price $8.50.

The title is self-explanatory.

"Applied Pharmacology (Clark)", by Andrew Wilson, M.D., Ph.D., F.R.F.P.S., and H. O. Schild, M.D., Ph.D., D.Sc.; Ninth Edition; 1959. London: J. & A. Churchill Limited. 8½" × 5¼", pp. 760, with 165 illustrations. Price: 50s. (English).

This book, originally by A. J. Clark, was last revised in 1952. Much of it has now been rewritten, and new chapters have been added.

"A Two-Year-Old Goes to Hospital: A Scientific Film Record", by James Robertson; Second Edition; 1959. London: Tavistock Publications Limited. 8½" × 7", pp. 28, with illustrations. Price: not stated.

A revised version of the guide to a film about a young child in hospital.

"Radioactive Sulphur as Benzidine Sulphate: A Methodological Study with Special Reference to S^{35}-Labelled Penicillin in Oral Surgery", by Erik Agren, *Acta Radiologica*, Supplement 166; 1958. Stockholm: Acta Radiologica. 9½" × 7", pp. 108, with 32 illustrations and 23 tables. Price: Sw.Kr. 30.

A study of methods in the analysis of distribution of radioactive penicillin in body fluids and oral tissues.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 12, 1959.

THE SECOND REPORT OF THE NATIONAL RADIATION ADVISORY COMMITTEE.

THE second report to the Prime Minister of the National Radiation Advisory Committee, July, 1959, which was laid on the table of the House of Representatives on August 19, 1959, is an informative and reassuring document. A summary of the report is published elsewhere in this issue (see page 375). We regret that we have not space to print the whole report, but there is not a great deal of importance in the report that is missing from the summary. However, a few points may, with advantage, be underlined and amplified. The hazards associated with exposure to ionizing radiation in X-ray diagnosis are brought firmly into perspective, as they now well may be. There was undoubtedly a stage when some clinicians used this aid to diagnosis too freely, and with little thought of the hazards involved; indeed, few people appreciated them fully at that stage. Then came the period of ultra-caution, with quite disproportionate but understandable fear on the part of many patients. Now the balanced statement of the report should have universal approval. On the other principal man-made source of radiation, global fallout, the report is reassuring. It is clear that Australia is particularly fortunate in the low fallout levels observed and need have no real fear on this score under present conditions. Concern that has been expressed in relation to the incidence of leukæmia, primary bone tumour and major genetic consequences would seem to have little to sustain it. One important aspect of this referred to in the report, but not included in the summary, is in recent studies relating to threshold doses of radiation. This whole subject has, of course, been particularly obscure and controversial, but the report states that considerable experimental support is being gained for the view that a certain radiation dose or threshold must be exceeded before any case of leukæmia will be induced. On the basis of the threshold dose accepted (in an alternative hypothesis) by the United Nations Scientific Committee, no cases of leukæmia could be caused by fallout in Australia from all weapon tests to date. A similar position would obtain for bone tumour. On the question of the influence of dose rate on the genetic effects of radiation, the Committee cites the work of W. L. and L. B. Russell and E. M. Kelly, which was published in the latter half of 1958. We quote the report:

> In summarizing their findings, these authors state that "from a practical point of view, the results indicate that genetic hazards, at least under some radiation conditions, may not be as great as those estimated from the mutation rates obtained from acute irradiation". The "some radiation conditions" referred to are those in which the total radiation dose to the gonads is received at a very slow rate in contrast to an acute or fast rate. Their findings would apply to irradiation of the gonads from fallout and, if confirmed by further studies, will mean that the slight genetic consequences given in the above evaluation [this presumably refers to the report of the United Nations Scientific Committee] would be reduced.

Another interesting question to which not much attention has been paid until recently is the biological significance of carbon 14. The report states that carbon 14 forms the same chemical compounds as the element carbon. It can therefore be incorporated into the structure of organic molecules and so become part of living tissue. It decays with a half-life of about 5600 years, emitting low energy beta particles. When embodied in tissue, carbon 14 can affect living cells. It occurs in nature, being produced by the absorption of cosmic ray neutrons in the nitrogen of the atmosphere. Its production and decay have been in equilibrium for some time, and it exists in man and his environment in essentially consistent quality. In the body it is responsible for about 1·5% of the natural radiation to which man is continuously exposed. Nuclear weapon explosions can lead to the production of carbon 14 through the absorption in nitrogen of the neutrons that are generated. These neutrons may result from fission or fusion reactions or, as in many high-yield weapons, from a combination of both. At present the radiation dose to the whole body from weapon-produced carbon 14 is about ½% of the natural background radiation from all sources. It will therefore be, according to the report, responsible for less than one-fifth of any biological effects caused in the future by naturally occurring carbon 14. It has still to be determined, however, what part, if any, carbon 14 plays in the production of biological effects and especially of mutations or other genetic effects.

The Committee makes something in the nature of a progress report on recommendations included in their first annual report. Referring to its previous warnings about care in the medical use of X rays, the Committee again stresses the fact that the use of X-radiation in medical practice is essential, and reaffirms its view that the medical use of X rays will remain the major man-made contributor to the radiation exposure of the Australian population if the associated great advantages to the community are not to be sacrificed. It is acknowledged that many responsible authorities and informed users of X rays in medicine are known to be making efforts through administrative and technical measures to reduce this exposure to a minimum consistent with medical necessity, and the Committee supports these efforts, strongly recommending their continued and more general application. On the question of the licensing of equipment to be used in medical diagnosis reference is made to the fact that the National Health and Medical Research Council has accepted its Medical Radiation Committee's recommendation that all X-ray equipment for use on man be registered, subject to its continual compliance with prescribed technical standards, and that this requirement for registration be introduced into the model legislation approved by the Council. The National Radiation Advisory Committee strongly supports this action taken by the Council and recommends that all

State governments be urged to legislate accordingly. It also strongly supports the proposed action of the National Health and Medical Research Council in seeking to have greater emphasis placed (both in medical and in auxiliary medical education in Australia) on the results of radiation exposure from the medical use of X rays, and also in taking steps to bring to the attention of users of X-ray equipment recommendations for minimizing radiation dosage during X-ray examinations. On the question of tuberculosis case-finding programmes involving the use of mass radiography, the Committee reaffirms its concurrence with the present policy in Australia to continue (with modern techniques and equipment) mass miniature radiographic surveys to meet requirements of public health. Referring to its recommendation that leukæmia should be declared a notifiable disease, the Committee notes that in November, 1958, the National Health and Medical Research Council endorsed this recommendation.

The first annual report of the National Radiation Advisory Committee, in which these matters were brought forward (this report was published in full in the issue of the Journal of August 23, 1958), was thought by some people at the time to arouse unnecessary fears, although it could not on any count be described as a sensational report, and it did in fact call attention to important matters and helped to get them into perspective. It may reasonably be said that the present report clarifies a number of the points which rightly or wrongly were criticized and brings the position up to date. Not the least part of its value, however, is its reference to important recent work which is not otherwise widely known.

Current Comment.

TREATMENT OF PNEUMOCOCCAL MENINGITIS WITH PANCREATIC DESOXYRIBONUCLEASE.

ALTHOUGH the pneumococcus is sensitive to many antibiotics, the mortality from pneumococcal meningitis remains very high. In a series of 800 patients from 14 clinics in the United States the mortality figures ranged from 8% to 68% with an average of 28%. All these were treated with penicillin and a sulphonamide. The high mortality has been attributed to the blocking effect of the inflammation exudate together with the septicæmia. Since the highly viscous exudate in the brain and spinal cord in pneumococcal meningitis contains a large proportion of polymerized desoxyribonucleoprotein, A. J. Johnson, J. H. Ayvazian and W. S. Tillett[1] have experimented with the intrathecal introduction of crystalline pancreatic desoxyribonuclease to liquify the exudate and render its absorption and removal easier.

Crystalline pancreatic desoxyribonuclease has been shown to be practically non-toxic when introduced either into the blood or intrathecally. In the present case the enzyme was given with penicillin. Twenty-five patients, of ages from four months to 87 years, were given penicillin intravenously and intramuscularly in doses ranging from 12,000,000 to 40,000,000 units per day. In six cases 5000 to 10,000 units of penicillin were given intrathecally on the first day. A sulphonamide was given for the first three or four days. The nuclease was given intrathecally daily to each patient for two or three consecutive days in amounts ranging from 50,000 to 1,000,000 units. Sometimes one or more further injections were given if the presence of pleocytosis continued. Doses of 1,000,000 units per injection gave no toxic symptoms. Sixteen of the patients were over 50 years of age, and 19 were over 40 years. It is usually considered that a bad prognosis should be given for patients over 40 years of age. Three of the 25 patients died during the period of observation, their ages being respectively 54, 62 and 75 years. Of the 64 patients treated in a similar manner in the same hospital without pancreatic desoxyribonuclease during the years 1951-1956, 24 died (37·5%). When the pancreatic enzyme was injected intravenously, small amounts diffused into the cerebro-spinal fluid, and in a few cases it was considered advisable to supplement the intrathecal injections with systemic injections. This was done for patients who responded slowly to treatment or who had evidence of cerebro-spinal block.

[1] *New Engl. J. Med.*, 1959, 260: 893 (April 30).

A LONG-ACTING VITAMIN B_{12} PREPARATION.

PARENTERAL administration of vitamin B_{12} has proved the most satisfactory method of administration in cases of pernicious anæmia. However, the very rapid absorption and urinary excretion following parenteral administration are considered to be limiting factors in its therapeutic usefulness, and a preparation of vitamin B_{12} which would be absorbed and excreted slowly would be very useful. R. E. Thompson and R. A. Hecht[1] have described a preparation which they claim fulfils these requirements in a very satisfactory manner. It was found that cyanocobalamin, zinc and tannic acid could be complexed to a very insoluble compound CZT. This has been put on the market as "Depinar". The experimental work was done at first on rats and later on human subjects. In the rats given 500 μg. of cyanocobalamin in the form of CZT it was found that there was practically no urinary excretion of the vitamin. This was shown also in human subjects. In human subjects the slowly absorbed vitamin B_{12} produces a marked elevation in the serum level of vitamin B_{12} which is sustained for 28 days or longer after a single 500 μg. injection. As there is at any time very little vitamin B_{12} in the serum, most of the 500 μg. injected is probably taken up by various tissues. Clinical studies in pernicious anæmia have confirmed the finding that vitamin B_{12} supplied in the form of CZT retains a biological activity equivalent to that of pure vitamin B_{12}. Another feature of the use of CZT is that much higher levels of the vitamin can be obtained and retained in the tissues, so that new studies can be made of the effects of a high "body pool" of vitamin B_{12}. It is suggested that doses of 500 μg. of vitamin B_{12} as CZT should be given at intervals of one to four weeks to keep up a high "body pool". It seems that the treatment of pernicious anæmia should be simpler with CZT.

[1] *Amer. J. clin. Nutr.*, 1959, 7: 311 (May-June).

GENETICS OF MICROCEPHALY IN MAN.

IN 1957 the Institute for Human Genetics in Münster, Westphalia, inaugurated an inquiry into pathological conditions in man based on mutant genes. W. F. Haberlandt undertook the problem of amyotrophic lateral sclerosis including progressive bulbar paralysis, whilst Gerhard Koch[2] investigated microcephaly (perhaps more correctly micrencephaly). The proportion of cases in mental hospitals turned out to be small, being of the order of one in 600 to 800; this can be explained by the high death rate in the first period of life. Among 23,000 children born in the Department of Gynæcology and Obstetrics in Münster only three were found to be microcephalic. Of these three, the condition of two had been caused by exogenous factors during fœtal life; this then gave one case of congenital microcephaly in 23,000

[2] *Acta Genet. med. (Roma)*, 1959, 8: 75 (January).

children. Altogether 106 cases were collected during one year. Patients with small heads associated with dwarfism or mongolism were excluded; other non-hereditary cases were those arising from various virus infections, particularly rubella, and also from vitamin deficiency and X-ray exposure. So far blood group incompatibility has not been detected as a causal agent. Of the 106 cases investigated only 36 appear to be hereditary. Consanguineous marriages were found in four families only. The report given is a preliminary one, and the tentative conclusion is reached that hereditary microcephaly is due to an autosomal recessive gene. The sex ratio here, as in other investigations, shows a remarkably even distribution. Further analyses in a wider field of population are being pursued, and the results will be awaited with interest.

FORECAST AND FOLLOW-UP.

THE Department of Social Medicine of the University of Amsterdam, under Professor A. Querido, has pioneered an interesting and important area of social medicine.[1] In a series of investigations an attempt has been made to determine the factors which affect convalescence and full recovery of patients discharged from a general hospital. The average doctor is aware that not a few patients fail to make the recovery expected, but he is often at a loss to know why. Querido and his team studied 1630 patients who passed through a municipal hospital in Amsterdam. It was a selected group, the excluded subjects being those younger than 15 or older than 65 years, those who on admission had an obviously poor prognosis, and those admitted for short periods as, for example, for tonsillectomy. Each patient was subjected to two types of evaluation: the clinical prognosis was determined in the ordinary way in terms of favourable-unfavourable and a psycho-social case history was prepared from which an integrative assessment of the patient was made. The history and assessment were in the hands of a team of three, a general physician, a social worker and a psychiatrist, whose work was parallel with but independent from the ordinary hospital team. Each member of this team took his own history, and the results were discussed by the team. The final conclusion sought was whether the patient was subjected to an unusual amount of stress-producing problems in his life, and if so to what extent he was capable of managing these problems. When it was decided that the patient was not able to handle his problems and was hampered by them, the term "distress" was used, implying that the psychic or social tensions were too heavy for the patient to bear. The term "somatic" was used to indicate that no distress could be detected or that the somatic illness was so great as to dominate the whole picture.

A follow-up investigation was made of each of the 1630 patients in his home about six months after discharge from hospital. This was done by a physician who knew the contents of the case history but was unaware of the psycho-social assessment. At the follow-up investigation patients were assessed as: (i) satisfactory—(*a*) free from complaint, (*b*) suffering from typical residual complaints (pain in scar) only, (*c*) free for a time of the original symptoms, although others not related to the illness for which he had been admitted to hospital had appeared; or (ii) unsatisfactory—(*a*) free from complaint for some time but now experiencing a return of the former symptoms, (*b*) suffering from complaints equal to or worse than before admission, (*c*) suffering a recurrence. The medical conditions suffered by the patients covered practically the whole range from malignant disease through the respiratory, circulatory and digestive diseases to accidents. For two conditions, diseases of the circulatory system and rheumatism, the unsatisfactory follow-up result was exceptionally high. If we omit these two conditions, no relation was found between the other clinical diagnoses and the condition at follow-up. The most outstanding feature was the comparatively low percentage of those with a favourable clinical prognosis who were rated satisfactory at the follow-up—660 out of 1128 patients. The incidence of "distress" among those with a favourable prognosis and a satisfactory follow-up was 24·7%, while the incidence among those with a favourable prognosis but an unsatisfactory follow-up was 64·1%. Distress was absent in 60% of those with an unfavourable prognosis but a satisfactory follow-up, and absent in only 31% of those with an unfavourable prognosis and an unsatisfactory follow-up.

This study shows that half the patients who clinically should have benefited from medical care did not do so because of social or emotional factors in their lives. In this respect an earlier study by the same group is informative. Weijel and Willemse[2] estimated that of 315 patients in a pilot study, 12% needed psychiatric consultation to establish a diagnosis and decide upon a programme of treatment, 15% needed supporting treatment by a family doctor, 41% needed after-care or case-work by a social worker, and 5% needed the care of a priest; these percentages are not additive. The numbers needing some form of help seem high according to our Australian services, but perhaps not according to the needs of patients.

[1] *Brit. J. prev. soc. Med.*, 1959, 13:33 (January).

WESTERN AUSTRALIA TODAY.

THE Western Australian Government has produced the first of a new series of handbooks[2] after a lapse of some 50 years. This first number sets a high standard of both production and content. A general historical review of the State is followed by descriptions of the physical features, climate, flora and fauna by experts in these fields from University and Museum. Some pleasing photographs are given, including one of Perth and two of the bush flowers in colour—Western Australia is justifiably proud of its *Leschenaultia biloba*, the most attractive of all Australian bush flowers. Chapters are devoted to government, vital statistics, social statistics, finance, land problems (including water conservation), production, trade and employment.

Some interesting details from the handbook may be mentioned. The distribution of population in Western Australia is determined largely by the availability of water, and so the population is almost wholly concentrated in the south-west corner from Geraldton to Esperance, where the average rainfall is about 30 inches, and in the Kalgoorlie goldfields area, which is supplied by pipe-line from Mundaring, near Perth, a distance of about 400 miles. The population increased slowly from the time of first settlement until about 1888, when the finding of gold caused the population to quadruple itself in twelve years. Western Australia is again enjoying a rapid increase of population, and this has caused a slight decrease in the proportion of persons aged 65 years and over. Crude birth rates have been high since 1947—about 25 per 1000 of population, as compared with 18 per 1000 in 1931-1935. Recently the crude death rate has been lower than elsewhere in Australia, but the infant mortality rate is slightly higher. Stillbirth rates are shown as 21 per 1000 in 1945 and 17 per 1000 in 1954. It comes as a surprise to many to learn that the total population of Western Australia now exceeds that of South Australia in, say, 1945. Thus the existence of the medical school is fully justified. Among the infectious disease notifications we observe that about 20 cases of typhus fever (Brill's) are reported annually, which seems a high figure. We look forward to further numbers in this series, and congratulate the Government Statistician on the production of this first volume.

[1] *"Mogelijkheden van intergraalgeneeskundig werk in het ziekenhuis"*, 1955, Amsterdam.

[2] "Official Year Book of Western Australia; 1957", issued under the authority of The Honourable Gilbert Fraser, M.L.C., Chief Secretary, by R. J. Little; 1958. Perth: Alex B. Davies, Government Printer. 9½" × 5½", pp. 382, with illustrations. Price: 10s.

Abstracts from Medical Literature.

ORTHOPÆDICS.

A Finger-Joint Prosthesis.

E. W. BRANNON AND G. KLEIN (*J. Bone Jt Surg.*, January, 1959) describe a metal-hinged type of prosthesis which they have developed for irreparably damaged joints of the finger, as an alternative to amputation or arthrodesis. The prosthesis is a replica of the normal joint and is used in the hope of restoring some degree of useful function to an otherwise useless part. Prerequisites for the use of this prosthesis are functionally restorable tendons, intact nerve supply, adequate circulation of the finger, and good motivation on the part of the patient. Complications consist of sinking-in of the prosthesis and loosening of the screw, and the authors suggest methods of counteracting these difficulties. In 10 out of 12 patients who were adequately followed up, a functional range of painless motion was restored, and the cosmetic appearance of the hand was improved. The authors work at a United States Air Force hospital, and they state that all patients returned to full military duty, and were engaged in occupations requiring use of the hands. They consider the results sufficiently encouraging to warrant further use of this procedure.

Dashboard Femoral Fracture.

S. J. RITCHEY *et alii* (*J. Bone Jt Surg.*, December, 1958) consider 263 fractures, treated at the Walter Reed Army Hospital, which were the result of automobile accidents and occurred between 1951 and 1957. Fifty-two of these were closed comminuted fractures of the shaft of the femur, and 19 were typical dashboard fractures. The others were associated with angular torsion. The authors consider the mechanics of this type of injury in some detail, especially the result of serious compression violence due to impaction of the knee against the dashboard. This is sometimes associated with jack-knifing at the hips and head and chest injuries against the steering wheel or the windscreen. It is noted that a two-hundred-pound man decelerated from 60 miles per hour to nothing, sitting with his knee two inches away from the dashboard, receives a force of 50 tons applied to the long axis of the shaft of the femur. Varieties of fractures occurred, depending on the angle of the leg at the moment of impact. Dislocation of the hip was often associated with local damage to the knee joint. If the patient was thrown into a twisted position long, spiral or oblique fractures occurred. When there was a direct blow on the leg open, comminuted fractures occurred. The authors compare the results of treatment by closed as against open methods of reduction. They note that with treatment by open reduction the period before unrestricted weight-bearing was longer than when the fractures were treated by closed methods. Also, only 6% of recoveries were classed as excellent after open reduction, as compared with the 50% of excellent recoveries among fractures treated by closed methods. The main reason for this considerable difference was the severity of complications which occurred after open operation, the worst of these being osteomyelitis. The heroic methods of reduction which were required to reduce the severe comminuted fractures, involving extensive surgery, led to a particularly high incidence of infection and also to delayed union. It was rarely possible to gain any time by this approach as the methods of fixation were rarely sufficient to allow early mobilization.

Traction Lesions of Brachial Plexus.

G. BONNEY (*J. Bone Jt. Surg.*, February, 1959), of the Royal National Orthopædic Hospital, London, discusses the prognosis in traction lesions of the brachial plexus in relation to 29 such lesions in patients seen at the hospital between 1949 and 1958. All but one of these patients were male, and most were between 16 and 25 years of age. The author states that recovery is always incomplete and even in the most favourable cases takes a long time, and that distressing pain is often a feature. The injuries were the results of motor-bicycle accidents in most cases, and were caused by severe force acting on the head or the body so as to extend the brachial plexus. Careful assessment of motor and sensory recovery showed that in this series there was no useful recovery of the extensor muscles of the wrist or the intrinsic muscles of the hand in any case. There was, however, recovery of the muscles round the shoulder, the trapezius, the rhomboids and the serratus muscles. Nineteen cases were followed up; the deltoid recovered in three of these, the lateral rotators of the shoulder in two, and the biceps in six. The series illustrated that recovery can begin up to 24 months after the injury. The author points out that this recovery in the shoulder, and occasionally in the flexors of the elbow, allowed the limb to be used to support articles in the axilla or to carry parcels. This function, as a rule, was better than the corresponding function of an artificial limb. The methods of making a prognosis are discussed in detail.

Associated Vascular Injuries in Orthopædic Surgery.

C. W. HUGHES (*J. Bone Jt Surg.*, December, 1958) reviews the problems that arise from injuries of vessels associated with soft tissue damage as well as with fractures. He notes the trend towards reconstruction of injured vessels and the avoidance of obliterative practices which were used generally during the Second World War. Arterial repair was much more commonly used under the conditions of the Korean War. He points out that the majority of these vessel injuries were not associated with fractures. They were commonly associated with nerve injury and other soft tissue damage. Writing from personal experience, the author notes that fractures of the pelvis were often associated with damage to the iliac arteries, and he reports that in other cases repair of vessels had followed operating room accidents after intervertebral disk surgery and manipulative reduction of fractures of the surgical neck of the humerus. In this case either the vessels had been in severe spasm, or the spasm was associated with a thrombus, or the vessels had been compressed or completely divided. He discusses the complications following vascular injuries, the most important being exsanguination leading to death or at least to severe shock. Shock causes vasoconstriction of the collateral circulation, which endangers the limb because of ischæmia and incipient gangrene. Ischæmia and possible gangrene are more likely if a tourniquet has been used, if the limb has been heated, or if vasoconstriction is not corrected by correct resuscitation. Another cause of ischæmia and gangrene is the swelling of ischæmic muscle after return of the flow of blood, which leads to tension in tight fascial compartments; other complications discussed are false aneurysms and arteriovenous fistulæ. The author devotes considerable space to the details of repair and considers the varying problems associated with this. Discussing arterial injury associated with fracture, he notes the difficulty of the problem, the importance of the injuries to bone and vessel being managed together, the help that an overriding fracture may give to the resuture of a divided artery, and the importance of avoiding tension after reduction of the fracture or extension of joints which had been flexed. He also warns against the use of plaster and of strapping extension.

Flexor Tendon Injuries of the Hand in Children.

J. L. BELL *et alii* (*J. Bone Jt Surg.*, December, 1958) discuss the results of their management of 60 children suffering from flexor tendon injuries of varying degrees. Some were associated with nerve injuries. Sixty-four operations were performed, of which 56 involved secondary repair. Secondary repair usually meant grafting, and except for one or two cases where palmaris longus was used the extensor tendon was taken from the toes. The technique of operation was the same as used in adults. Occasionally anæsthesia was necessary for the removal of the stitches. No physiotherapy was ordered. The results are considered and it is thought that generally recovery was better than in adults. The authors stress that consideration must be given to the extent of the damage to the joints and surrounding tissues when assessing the final results of tendon grafting. Serious damage leads to extensive scarring and poor results.

Restoration of Flexors of the Elbow.

D. M. BROOKS AND H. J. SEDDON (*J. Bone Jt Surg.*, February, 1959) describe a new operation for the restoration of function in cases of paralysis of the elbow, by the use of a pectoral muscle transplant. In this, the long tendon of the paralysed biceps is used to allow the pectoral muscle to flex the elbow. The belly of the paralysed muscle is left in the connecting tendon. Biopsy specimens taken at two and at 15 months after operation show that as a result of ischæmic changes in the belly of the biceps this turns into white tough fibrous tissue, microscopically indistinguishable from normal tendon. Details

of 10 cases are given (in four the paralysis was due to poliomyelitis, in five to brachial plexus injury, and in one to arthrogryposis multiplex); in six the resulting function was described as excellent or good; in two it was fair, and in two the result was a failure. In the cases of failure, this was due to the pectoralis major being too weak. In some cases stabilization of the shoulder joint improved the strength of the function of the pectoral muscles.

Orthopædic Management of Neuropathic Joints.

R. L. SAMILSON *et alii* (*A.M.A. Arch. Surg.*, January, 1959) discuss the treatment of Charcot's joints in a total of 55 patients with 87 affected joints. Tabes dorsalis was the cause in 42 patients, syringomyelia in four patients, diabetic neuropathy in four patients, alcoholic neuropathy in one patient, while in four patients the cause was unknown. The authors consider that the satisfactory management of neuropathic joints requires early diagnosis and an early attempt at arthrodesis. They noted that the successful fusions were obtained when less than five years had elapsed between the onset of joint symptoms and arthrodesis, whereas the unsuccessful cases were chiefly those in which arthrodesis was performed more than five years after the onset of the symptoms. At least eight months were required for clinical and radiological evidence of bone fusion.

PÆDIATRICS.

Hæmadsorption Viruses and Respiratory Illness in Childhood.

R. M. CHANOCK *et alii* (*J. Amer. med. Ass.*, February 7, 1959) report a study of the relationship between hæmadsorption viruses and respiratory illness in childhood involving 1738 children who were patients in three Washington hospitals. Types 1 and 2 hæmadsorption viruses were recovered almost exclusively from patients with respiratory disease. Both viruses were recovered from children with mild illness as well as from persons with respiratory disease severe enough to require admission to hospital. The results suggest that these agents play an ætiological role in respiratory illness. The virus recovery rate among patients with respiratory disease was 2·3% for type 1 and 3·9% for type 2. The amount of illness associated with these agents was higher (19·5%) when estimated by the complement-fixation technique. The highest rate of virus recovery (16·7%) or complement-fixing antibody rise (30·2%) occurred for type 2 virus in patients with the croup syndrome.

Acquired Hæmolytic Anæmia.

J. HARLEY AND L. DODS (*Aust. Ann. Med.*, May, 1959) discuss acquired hæmolytic anæmia of childhood with particular reference to the case records of eight children seen at the Royal Alexandra Hospital for Children, Sydney. Four of the eight children were of Mediterranean racial extraction. The onset of the illness was usually abrupt; on admission to hospital each of the patients appeared to be seriously ill, and in every case the anæmia was severe. Recovery from the illness was complete in each case; in seven cases the duration of the hæmolytic episode was less than four weeks, but in the eighth case excessive hæmolysis persisted for more than two years. The authors state that it has been suggested that a constitutional anomaly of erythrocytes—namely, glutathione deficiency—is essential for the development of acquired hæmolytic anæmia following the ingestion of broad beans, sulphonamides or para-amino salicylic acid, and that this defect is probably hereditary. They determined the glutathione content of the erythrocytes of one patient who was considered to have suffered from favism, and found that this was significantly reduced one year after the patient's recovery from his illness. The significance of glutathione deficiency of the erythrocytes in such cases is discussed.

Acute Glomerulonephritis with the Nephrotic Syndrome.

S. WILSON AND W. HEYMANN (*Pediatrics*, May, 1959) describe five cases in children of acute post-streptococcal glomerulonephritis associated with mild and transient nephrotic syndrome. At the beginning of the illness each patient developed more marked œdema than is usually seen, marked proteinuria, hypoproteinæmia with hypoalbuminæmia, and hyperlipæmia, and thus presented the characteristic features of the nephrotic syndrome. These symptoms were noted in each case for not longer than three to 10 days. A diagnosis of acute glomerulonephritis was established by the short duration of the disease (one to two months), the presence in four of the five patients of elevated titres of antistreptolysin "O", the presence of beta-hæmolytic streptococci in throat cultures, and follow-up examinations which showed that all had recovered completely without exacerbations. No implication is made by the authors that the nephrotic syndrome of infants and children is ætiologically related to acute glomerulonephritis. They conclude that mild nephrotic syndrome may complicate approximately 4% to 5% of cases of acute glomerulonephritis in children.

Aminophylline Poisoning.

H. BACAL *et alii* (*Canad. med. Ass. J.*, January 1, 1959) state that while physicians generally are aware of the therapeutic value of aminophylline in the management of bronchial asthma, less widely known, discussed or even recognized is aminophylline poisoning arising from its therapeutic use. They present 10 cases of therapeutically induced aminophylline poisoning observed at the Montreal Children's Hospital over a period of five years, and illustrate the more usual clinical course of aminophylline poisoning in children. Eight of the 10 cases followed administration of aminophylline by the rectal route, and in one case the drug was administered intravenously. The early recognition of aminophylline poisoning, often difficult, may prevent severe morbidity or even death. Particular early symptoms are unusual irritability, excitement and vomiting. Later, hæmatemesis and dehydration occur, along with tremors, epileptiform convulsions, drowsiness and coma, while finally cardio-vascular collapse and death ensue. Treatment of the intoxication is purely symptomatic, aimed at sedation, support of respiration and circulation, and the prompt prevention or correction of dehydration. While the question of idiosyncrasy versus intoxication is far from settled, it is the authors' view that overdosage rather than hypersensitivity is the causative factor. The following dosages are recommended in the use of aminophylline in the treatment of bronchial asthma in children: oral suspensions and tablets, 5 mg. per kg. of body weight, repeated if necessary every eight hours, but not more often than every six hours; rectal suppository or retention enema, 7 mg. per kg. body weight, repeated every eight hours, but not more often than every six hours, and restricted to cases in which oral administration is not practicable. No undesirable effects have been encountered with this regimen, which has been found adequate for treatment of asthmatic children exclusive of those in status asthmaticus.

Infants of Diabetic Mothers.

S. S. GELLIS AND D. YI-YUNG HSIA (*A.M.A. Amer. J. Dis. Child.*, January, 1959) review the available literature on the outcome of pregnancy in diabetes and their personal experience with 934 pregnancies in diabetic mothers. They note that pregnancy failures are several times more common among diabetic women than in normal women, and that this excess loss is limited almost exclusively to the period after the twenty-eighth week of pregnancy. There is little indication of any significant decrease in this loss in recent years, and experience and teamwork seem to be the only factors which influence the ultimate outcome of such pregnancies. Only two material factors appear to influence the fœtal mortality rate, namely the severity of the diabetes and good diabetic control. There is no proof that the administration of female sex hormones significantly reduces the fœtal mortality rate. Ideally, infants of diabetic mothers should be delivered between the thirty-fifth and thirty-sixth weeks of gestation. The authors found no evidence that the mode of delivery significantly affects the outcome. In their own series, among 755 viable fœtuses there were 56 intrauterine and 93 neonatal deaths. They find that, in the neonatal period, respiratory distress is clinically the principal complication. At autopsy, pulmonary hyaline-membrane disease and atelectasis are the only findings in two-thirds of the infants who die. Hypoglycæmia, infections and congenital anomalies make a relatively minor contribution to the mortality figures. The authors find that no specific measures are helpful in the prevention or treatment of hyaline-membrane disease, and that reliance must be placed on good pædiatric care and general supportive measures. They conclude that no rational mode of treatment for the infant of the diabetic mother is likely to emerge until the maternal and fœtal factors responsible for hyaline-membrane disease are better understood.

Special Article.

THE EFFECTIVENESS OF VACCINATION IN PREVENTING POLIOMYELITIS IN AUSTRALIA OVER A PERIOD OF TWO YEARS.[1]

BEFORE proceeding to the poliomyelitis vaccination campaign in Australia, the Commonwealth Department of Health appointed a Surveillance Committee to assist in the Department's general oversight of the campaign. The Committee's main functions were to set up working diagnostic criteria for poliomyelitis, to investigate suspected cases of poliomyelitis in vaccinated subjects and, if possible, to assess the effectiveness of the Australian poliomyelitis vaccine (Salk type) in preventing poliomyelitis by studying the incidence of cases in vaccinated and unvaccinated individuals as the campaign progressed. Antibody response levels in suitable groups of vaccinated persons were also to be studied for the same purpose simultaneously by the Commonwealth Serum Laboratories, Melbourne (C.S.L.). A field trial along the lines carried out in the U.S.A. was not considered essential, since the American trial had adequately shown that the vaccine was protective (Francis *et alii*, 1955).

At the outset, the Surveillance Committee issued a statement on diagnostic criteria to assist uniform recording of poliomyelitis throughout Australia. A special surveillance form, based on that described by Francis (*loco citato*) was designed to record details of every suspected case of poliomyelitis occurring in Australia after July 1, 1956. Obligation to notify cases of poliomyelitis in accordance with State Health Regulations continued as formerly.

The various State medical bodies concerned were asked to arrange collection of suitable faecal and serum specimens from suspected cases in vaccinated persons at the earliest possible time during the acute phase. It was also requested that a convalescent serum specimen be taken six to eight weeks after the onset of the disease. Specimen units and instructions for the collection and transport of specimens to the testing laboratories in Melbourne and Adelaide were made available by the C.S.L.

Intensive vaccination in Australia was commenced towards the end of June, 1956. The initial immunization consisted of two intramuscular injections of C.S.L. poliomyelitis vaccine (Salk) given four weeks apart. Third booster doses were given seven to 15 months later. Apart from pregnant women and medical, nursing and laboratory personnel at special risk, vaccination was restricted to children aged from six months to fourteen years inclusive. Of these children, about 90% had been vaccinated by the end of June, 1958, 2,129,000 having received the full course, 378,000 two injections and 74,000 one injection.

At the commencement of the campaign some public concern existed about the safety of the vaccine; this was aroused by the unfortunate incident in the U.S.A., where some of the children inoculated with certain lots of poliomyelitis vaccine (prepared by one manufacturer) developed clinical poliomyelitis. The latter was subsequently shown to be due to faults in the vaccine. To reassure the public and ensure the success of the campaign, it was imperative that every suspected case of poliomyelitis in a vaccinated person in Australia should be immediately and fully investigated. As a result of this emphasis, it is believed that all suspected cases in vaccinated persons were examined either by the Surveillance Committee or by a State poliomyelitis authority or specialist, through whom details were conveyed to the Surveillance Committee.

Safety of the Vaccine.

The data recorded on all surveillance forms were carefully evaluated by the Committee, which was in continuous operation. The Committee accepted as poliomyelitis 22 cases in vaccinated persons over a period of two years from the commencement of vaccination on a large scale. Eleven of these patients had received one injection only, and of these, two were ill prior to vaccination, two became ill within two days of vaccination, and in the others symptoms were first noticed at five, seven, 26, 28, 34, 36 and 350 days after vaccination. Of those cases which occurred in subjects who had received two injections, symptoms first developed in from two to 14 months after the first dose of vaccine.

In the U.S.A. incident referred to earlier, the cases attributable to the vaccine were concentrated in the period four to 14 days after vaccination, and from eight to 28 days for uninoculated family contacts (Langmuir, Nathanson and Hall, 1956). It is justifiable to assume from these facts that in at least four of the Australian cases in vaccinated subjects, infection had occurred prior to receipt of vaccine. In none of the four cases occurring within a week of vaccination was the injected limb the first site affected by paralysis, whereas in the American series there was close correlation between the site of inoculation and the first paralysis.

From the month-by-month attack rate in unvaccinated children and the relative numbers at risk in each period, a statistical estimate was made of the number of cases which might be expected in vaccinated subjects during the first post-vaccinal week, on the assumption that it was then too early for the vaccine to exert protection. The estimate and the observed number of cases were the same—i.e., four cases.

From these figures it seems reasonable to state that in the two-year period, during which about 8,000,000 injections of poliomyelitis vaccine (C.S.L.) were given, no evidence has emerged that the vaccine has caused or provoked poliomyelitis.

Effectiveness of the Vaccine.

Assessment of the effectiveness of vaccination against poliomyelitis in Australia was made difficult by the fact that data available for cases occurring in unvaccinated individuals were often less complete than data recorded for the vaccinated. This has unfortunately affected the validity of comparisons of incidence between the two groups.

All available information, including laboratory data relative to each suspected case occurring in Australia over the two-year period, was examined as objectively as possible by the Surveillance Committee before the case was rejected or accepted. It was thought that a useful comparison between cases in vaccinated and unvaccinated groups could be made from the data, provided that it was made clear that equally complete information was not available for both groups as would be obtained, for instance, by a properly controlled field trial.

Details relative to all Australian cases accepted as poliomyelitis by the Surveillance Committee in the two years following the commencement of the vaccination campaign are set out in Table I.

Among the cases accepted, the proportion of non-paralytic cases in the two groups was approximately the same—three out of 22 for the vaccinated and 40 out of 234 for the non-vaccinated. For this reason the calculations in Table II, which compares actual with expected incidence in the vaccinated group, have been based on all cases accepted by the Committee, whether paralytic or not. Obviously there were too few non-paralytic cases to permit a separate useful analysis.

Of the 22 cases in vaccinated subjects, six occurred within one week of the first dose—too soon for the patients to have had any chance of protection by the vaccine—and one of the subjects received vaccine not made in Australia. These seven cases have been excluded from the assessment, as they provide no information on the protection afforded by C.S.L. poliomyelitis vaccine.

Of the remaining 15 vaccinated persons who contracted poliomyelitis, all of whom were children, five had received one dose of vaccine only and 10 had received two doses. These numbers are too small to permit any useful comparisons of the relative protection afforded by one or two doses of vaccine. However, when exposure periods are taken into account, the small difference observed can be shown to favour increased protection afforded by two doses.

By the end of June, 1958, more than three-quarters of those vaccinated had received the full series of three injections, without a single case of poliomyelitis in the group.

At the start of the campaign the natural incidence of poliomyelitis in Australia was falling, and it continued to fall during the period under investigation. At the same time, the proportion of vaccinated subjects increased sharply. These changing circumstances prevented the use of simple averages in comparing the vaccinated and unvaccinated groups. The main problem thus was how much, if any, of the fall in incidence was due to vaccination.

Difficulties arising from the changing incidence, and also the differences between the States, were overcome by

[1] Prepared by J. J. Graydon, D.Sc., of the Commonwealth Serum Laboratories, from information supplied by the Poliomyelitis Vaccination Surveillance Committee.

TABLE I.

Poliomyelitis Cases in Australia Accepted by the Surveillance Committee by States for the Period July 1, 1956, to July 30, 1958.

State.	Vaccinated Subjects Contracting Poliomyelitis.				Unvaccinated Subjects Contracting Poliomyelitis.	
	Vaccinated Presumably Whilst Incubating Poliomyelitis.[1]	Received One Dose of Vaccine.	Received Two Doses of Vaccine.	Received Three Doses of Vaccine.	Aged 0 to 14 Years.	Aged over 15 Years.
Western Australia	—	—	—	—	2	3
South Australia	3	1	1	—	29	34
Victoria	—	—	4	—	17	12
Tasmania	1[2]	—	2	—	19	11
New South Wales	1	1	2	—	41	33
Queensland	1	3[3]	2	—	17	16
Australia (total)	6[2]	5[3]	11	—	125	109

[1] Onset of illness within seven days of the subject's receiving the first dose.
[2] The only case in a vaccinated subject aged over 15 years occurred in Tasmania.
[3] Includes one patient vaccinated with Salk vaccine not made in Australia.

treating the data as follows. On the null hypothesis that vaccination had exerted no protective effect, one would expect the same proportion of cases to numbers at risk in both vaccinated and unvaccinated groups in any one period (say, one month). On this basis, the number of cases to be expected among those vaccinated could be calculated from the proportion of cases which occurred in the unvaccinated group. Separate calculations were made for each month and for each State, the numbers in the vaccinated and unvaccinated groups at each stage being taken into account. The expectancies so obtained were added for the whole of Australia for the full two-year period, and compared with the number of cases which occurred in vaccinated persons during the same period (see Table II).

If there had been no protection due to vaccination, one would expect 87 cases among vaccinated children aged under 15 years, whereas the actual number was 15. Statistically this difference is highly significant ($P < 0{\cdot}001$), which proves that the null hypothesis is invalid, and that vaccination has resulted in significant protection. The best available estimate of the degree of protection is 72/87 or 83%.

Over most of the period under review, less than 2% of the total population aged over 15 years had been vaccinated, and this percentage was reached only toward the end of the period, when the general incidence of cases had fallen to a very low figure. Consequently, it was not considered profitable at this stage to attempt statistical comparison between the vaccinated and unvaccinated groups aged over 15 years, but it is expected that this group will yield comparisons of special value in the next few years. The only vaccinated person aged over 15 years who contracted clinical poliomyelitis was a nurse in an infectious diseases hospital, who was exposed to the risk of infection from patients in the hospital. As she became ill within a week of receiving her first dose of vaccine, insufficient time would have elapsed for the development of useful protection, and she may have been incubating the disease at the time of injection. There were 109 cases in non-vaccinated persons aged over 15 years in the same two-year period.

Attention is drawn to the observation that in the whole of Australia there were only six cases of poliomyelitis in children aged under 15 years during the 12 months' period ended June 30, 1958, compared with 16 cases in persons aged over 15 years.

Summary.

1. Before the commencement of large-scale immunization of children with Australian poliomyelitis vaccine (C.S.L.), the Surveillance Committee set up satisfactory diagnostic

TABLE II.

Comparison of Cases of Poliomyelitis Observed and Expected in Vaccinated Children Aged up to 15 Years by States.

Month.	Western Australia.		South Australia.		Victoria.		Tasmania.		New South Wales.		Queensland.		Australia.	
	O.[1]	E.[2]	O.	E.	O.	E.	O.	E.	O.	E.	O.	E.	O.	E.
August, 1956	—	—	—	1·38	—	0·16	—	0·80	—	0·06	—	0·09	—	2·49
September, 1956	—	—	—	1·10	—	0·15	—	0·12	—	0·40	—	1·42	—	3·19
October, 1956	—	—	1	1·79	1	0·36	—	—	—	—	1	0·56	3	2·71
November, 1956	—	—	—	—	—	*0 61*	—	—	1	1·38	—	2·43	1	4·42
December, 1956	—	—	—	1·44	1	0·39	—	—	—	4·67	—	—	1	6·50
January, 1957	—	—	1	—	1	0·50	—	—	—	0·84	—	4·06	2	5·40
February, 1957	—	2·26	—	1·96	—	—	—	—	—	5·07	1	2·51	1	11·80
March, 1957	—	—	—	—	—	—	1	—	—	*4·24*	*1*	*1·56*	2	*5·80*
April, 1957	—	—	—	2·37	—	—	—	—	—	3·27	1	—	1	5·64
May, 1957	—	—	—	—	—	—	—	7·26	—	7·05	—	—	—	14·31
June, 1957	—	—	—	—	—	—	—	7·26	1	3·08	—	—	1	10·34
July, 1957	—	—	—	—	—	—	—	—	—	4·04	—	—	—	4·04
August, 1957	—	—	—	—	—	—	1	—	—	—	—	—	1	—
September, 1957	—	—	—	—	—	—	—	—	—	—	—	—	—	—
October, 1957	—	—	—	—	—	—	—	—	—	—	—	—	—	—
November, 1957	—	—	—	—	—	—	—	—	—	—	—	—	—	—
December, 1957	—	—	—	—	1	—	—	—	—	—	—	—	1	—
January, 1958	—	—	—	—	—	—	—	—	1	—	—	—	1	—
February, 1958	—	—	—	—	—	—	—	—	—	—	—	—	—	—
March, 1958	—	—	—	—	—	—	—	—	—	—	—	—	—	—
April, 1958	—	—	—	—	—	—	—	—	—	9·93	—	—	—	9·93
May, 1958	—	—	—	—	—	—	—	—	—	—	—	—	—	—
June, 1958	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	—	2·26	2	10·04	4	2·17	2	15·44	3	44·03	4	12·63	15	86·57

[1] O. = Observed cases accepted by the Surveillance Committee.
[2] E. = Cases expected in vaccinated subjects if the incidence was the same as in the unvaccinated. (Each month and State calculated separately to allow for changing incidence and changing proportion of population vaccinated.)

criteria to facilitate uniform recording of poliomyelitis in Australia.

2. During a two-year period to June 30, 1958, about 8,000,000 injections were given, mostly to children aged under 14 years. Of the latter, 2,129,000 had received the full course of three injections, 378,000 two injections and 74,000 one injection.

3. No evidence has emerged of the vaccine's having caused or provoked paralysis.

4. During the period under investigation there were 256 cases of poliomyelitis accepted by the Surveillance Committee. Of these patients, 146 were children aged 0 to 14 years, of whom 21 had received one or two doses of vaccine, and 110 were aged over 15 years (one vaccinated).

5. Immunization with C.S.L. vaccine was about 80% effective in preventing poliomyelitis in the same period.

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Addendum.

In Australia, since June, 1958, there have been 75 cases of poliomyelitis confirmed by the Surveillance Committee. Of these, 65 occurred in Victoria in the course of a sporadic outbreak which started in late July in the western and northern suburbs of Melbourne.

In vaccinated children (0 to 16 years) there have been 13 cases; six of the patients had received three injections of vaccine, three two injections and three one injection. One girl was vaccinated on the day when symptoms were first noticed, and she could not, therefore, be regarded as representing a case in a vaccinated person. There were 42 cases in unvaccinated children of the same age group.

Since June, 1958, the proportion of vaccinated children has remained fairly constant in each age group, and has ranged from about 25% in the 0 to 1 year group to over 90% in those of school age, falling away again to about 33% in those aged 16 years.

If the incidence of poliomyelitis at each level had been the same in vaccinated children as that observed in the unvaccinated, about 180 cases would have occurred in vaccinated children, whereas there were actually 12 cases. This suggests that the vaccine gave a higher degree of protection (over 90%) in the last six months than that reported above for the first two years of the campaign.

The improved protection rate may have been due to the larger proportion of the group who had received their third or "booster" injection during the later period. By June, 1958, about 85% of those vaccinated had received their full course of three injections, and in these the incidence of poliomyelitis was much lower than in those who had received one or two injections only.

There were 20 cases in adults, none of whom had been vaccinated.

It is evident that extensive vaccination has favourably influenced the course of the current outbreak of poliomyelitis in Victoria.

British Medical Association.

NEW SOUTH WALES BRANCH: SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held in the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, on July 31, 1958, the President, DR. A. W. MORROW in the chair.

Kuru.

A black and white sound film was shown dealing with kuru and its investigation in New Guinea.

Resuscitation of the New-Born.

DR. R. D. MACBETH read a paper on the resuscitation of the new-born presented from the viewpoint of the obstetrician.

He began by saying that there were many moments of anxiety in the life of an obstetrician and that not the least of those was the few minutes after a baby was born. It was his responsibility to get the baby breathing. No pædiatric specialist was there on the spot at 3 a.m., and no bronchoscopist—the burden was laid on him to see that breathing was initiated. Later, possibly, the pædiatrician might be called upon to see that respiration continued normally. It was with the obstetrician's part in this resuscitation of the new-born that he was concerned that night.

Dr. Macbeth said that it was known that the fœtus had rhythmic, slow respiratory movements, while still in utero, but it was most unusual that enough liquor reached the smaller air sacs of the fœtal lung to expand them. If, however, the fœtus was distressed during labour and became anoxic it might inhale a lot of liquor. However, physiologists agreed that intrauterine respiratory movements did not just continue when the baby was born. Atmospheric breathing had to be initiated and established by specific stimuli. Under normal birth conditions the cutaneous and proprioceptive stimuli of cold and touch and movement of joints, stimulated the medullary respiratory centres to initiate rhythmic breathing movements. At first these were usually diaphragmatic and very shallow, the chest wall might not be seen to move and the air passed down only to the smaller air passages. As the child awakened further, it cried and inhaled powerfully, and unstuck the alveolar walls over large areas of the lungs. That initial expanding force might be as much as 20 to 35 centimetres of water. Once the alveoli were opened, a much smaller expanding power was needed to maintain respiratory alveolar filling. That was probably not more than five to 10 centimetres of water. After the first vigorous gasps and cries, the child settled down to a quiet abdominal breathing and remained pink.

Dr. Macbeth went on to say that if the child was somewhat asphyxiated the higher medullary centres were not able to respond to the cutaneous and proprioceptive stimuli and the child became progressively cyanosed. When anoxia reached a certain level the carotid sinus receptors initiated a more primitive type of gasping respiration. The child took several deep gasps and under favourable conditions, this opened some alveoli, some oxygen entered the blood, and the anoxic medullary centres receiving oxygen were activated and able to respond and set up the normal respiratory rhythm. If gasping movements became more feeble and more than 30 seconds apart after about 10 minutes from the time of birth, the outlook was grave and pointed to gross damage of the medullary centres, either from trauma or from severe oxygen lack. In adults the chemoreceptors in the carotid sinus responded to carbon dioxide in the blood. It was not appropriate to give carbon dioxide, however, in neo-natal asphyxia as there already was an excess in the blood. Fortunately the newborn child was specially equipped to withstand a degree of anoxia which would be fatal to a baby of a few days old and even more so to adults. The factors which made this possible were probably a low cerebral metabolic rate and a capacity for anaerobic metabolism of sugar. If anoxia continued too long and the child survived, it might show permanent damage to the highest brain centres and be mentally retarded, or even spastic.

Dr. Macbeth then said that the factors which determined whether a baby would need resuscitation or not were usually present long before it was born. They lay in the management of the labour and delivery. The child would undoubtedly need skilful resuscitation if the mother had been very heavily sedated until the last stages of labour, or if fœtal distress was allowed to continue without delivery, or if the delivery itself was traumatic and the baby had sustained intracranial damage. Sedatives and anæsthesia were kept to a minimum especially if the baby was premature. If morphine or pethidine had been given in big doses near to the time of delivery, "Lethidrone" was given to the mother before delivery and into the umbilical vein of the baby if it was slow to breathe. "Lethidrone" had no effect in counteracting the inhalation anæsthetics or other sedatives. For the delivery of premature babies he usually employed local anæsthesia and allowed trilene to reduce the pain of labour. He had often thought that the babies born in the ambulance or just on the mother's arrival in hospital were in the best "crying condition". They had had no sedation whatsoever. If there were signs of intrauterine fœtal distress, which was almost always a sign of anoxia, he gave intranasal oxygen to the mother. This, he thought, did improve the condition of the fœtal heart. It had been mentioned that the fœtus was able to metabolize sugar anaerobically. With this in mind, some gave 25% dextrose solution intravenously to the mother if there was fœtal distress and delivery was not possible in a short time.

Dr. Macbeth then discussed the problem of the extraction of mucus. He said that as soon as the baby's head was

delivered mucus was seen to pour from the mouth and nostrils. This occurred naturally as the chest was compressed by the pelvic walls and the uterine contractions. Probably the most important single act of resuscitation was to suck the nostrils and naso-pharynx clear of that thick mucus immediately the head was delivered through the vulva, before proceeding to the completion of the delivery. A very mobile type of sucker was needed to get into awkward places. He suggested that the most useful type was the small rubber bulb hand sucker, or an oxygen vacuum sucker with a long light rubber tube. When a breech was delivered, as soon as exposure of the mouth was possible, the assistant should suck out the mucus. There was then no need for haste as long as the mouth was kept exposed for breathing. In Cæsarean section the same applied—as soon as the mouth was exposed liquor must be sucked out. That was even more important than in a normal delivery as there was no chest or abdominal compression and the Cæsarean baby often had large amounts of fluid in the respiratory passages and the stomach. When the child was fully born, it was at once held head down at an angle of about 30 degrees with the horizontal, the air passages and the naso-pharynx and nostrils were again sucked out and the stomach was aspirated, especially in cases of Cæsarean section.

Dr. Macbeth went on to say that, as he had pointed out, the first gasp was the most powerful one and was the mechanism for opening the alveolar spaces. If this first gasp carried down into the lung the mucus and debris lying in the mouth and nose, the child might die of asphyxia or later develop emphysema or broncho-pneumonia. After the first few breaths, when the alveolar walls had become unstuck, it was found that the fluid in the bronchial tree began to travel towards the trachea and appeared in the naso-pharynx, so that after a few breaths had been taken it was necessary to suck out the baby's air passages again and clear them of fresh mucus. After the lungs had expanded, the pulmonary circulation greatly increased and much of the fluid in the lung was rapidly absorbed.

Dr. Macbeth then discussed the administration of oxygen. He said that oxygen to the newborn could be life saving, but its administration could also be the cause of the infant's death. If respiration was not established within two or three minutes and the baby was becoming more cyanosed, a nasal catheter was passed to about one and a half inches from the external nares, and oxygen was run into the naso-pharynx at about one and a half litres per minute. The stimulation of the catheter being passed into the nose itself would often excite respiratory movements. The presence of pure oxygen at the glottis would mean that on the first breath the baby could get pure oxygen. That was the method in general use and most obstetricians refrained from the more vigorous methods of forcing oxygen into the baby. However, there were occasions when, in the hands of an expert, it was safe and perhaps life saving to use oxygen administered under positive pressure, or by the intratracheal route, or by the intragastric route. However, he wanted to emphasize most strongly that all those other methods of giving oxygen had been fraught with danger and damage to babies on many occasions, and he considered that they should be used only in the hands of really expert people.

Dr. Macbeth then referred to the use of oxygen administered by the intragastric route. He said that probably the least dangerous method of administering oxygen, other than by the intranasal route, was to give it by the intragastric route through a small catheter, passed about 17 or 18 centimetres from the mouth into the stomach. A similar catheter was passed beside it at the same time and acted as an escape route for the oxygen. The end of this second catheter was put under water and the stream of bubbles could be observed. The oxygen was run in at the rate of about two litres per minute and frequently it was noticed that the small intestine, as well as the stomach, very quickly filled up with oxygen and some was passed *per rectum* within a very few minutes. The idea of the method was to give a small absorption of oxygen in order to activate the medullary respiratory centres, so that they would respond to stimuli, and commence the normal respiratory movement. It might be said there, however, that there was considerable doubt in the minds of a number of physiologists whether enough oxygen was absorbed in this way to be of any real value.

Dr. Macbeth then discussed the intratracheal insufflation of oxygen. In this procedure the infant was placed on his back with the head somewhat extended and was carefully intubated with a small blunt tipped catheter, under direct vision with an infant laryngoscope. That could be quite gently done and should not cause damage or distress to an infant if the operator was expert. The catheter was passed about one or two inches into the trachea and oxygen was run in at the rate of one litre per minute. It was ideal to have a bag attached to the system and a manometer gauge in the circuit, so that, by pressure on the bag, a pressure of not more than 20 centimetres of water was applied. That would not open the alveoli initially but would give some absorption of oxygen from the walls of the larger air spaces. Another catheter might be passed through the glottis to give an escape route for the oxygen, but that was not always used. He thought that that method did run some risk of pulmonary emphysema or rupture of the lung. From a study of a large number of post-mortem specimens it was alarming to find how many babies had damaged lungs, probably as a result of over-vigorous resuscitation. Many cases of interstitial pulmonary emphysema and rupture of lung alveoli with pneumothorax were found. It was difficult to see emphysema in the X-ray picture of an infant's lung and it was never known how many babies did suffer some degree of that type of damage, and yet survive. Emphysema or rupture of the lung occurred as a result of distension and distension was a product of the pressure and volume of the gas. It had been experimentally demonstrated that if the pressure was applied over a very short period of time, the effect of distension did not occur. Day had shown that if a pressure of up to 40 centimetres of water were applied to the lung over a period of time not greater than 0·2 of a second, then no rupture of alveoli or occurrence of interstitial emphysema would happen, but this type of damage often did occur if the pressure was applied for more than 0·4 of a second. This theory had been applied by several workers to apparatus used in the resuscitation of infants, and if used under perfect conditions probably the results were good. However, he was sure that once the initial stage of the unsticking of the alveoli occurred, then the high pressure should be reduced immediately to the low pressures found necessary to maintain the normal lung expansions. He personally considered the method dangerous. Another dangerous method was that of putting a nasal catheter in and holding the mouth and nose closed for an indefinitely short period of time and then releasing it. The older obstetricians had done this frequently and distension of the stomach used to occur and there had been cases when the lung had burst. At the Women's Hospital, Crown Street, they had also used an infant size Drinker type of apparatus to resuscitate infants who were in a collapsed condition and not breathing. However, they considered that this equipment had damaged the lungs of a number of babies and they had ceased its use.

Dr. Macbeth then said that in order to establish that it was not just an impression that the positive pressure type of equipment was damaging to an infant, he had asked Dr. Moyes, the pathologist at the Women's Hospital, Crown Street, to give him certain figures from the post-mortem room. In the 18 months period from August, 1956, to January, 1958, there had been 103 autopsies on live-born infants. Eight of these infants had shown varying degrees of pneumothorax at necropsy. In 27 pulmonary emphysema had been either the major or a major cause of death. A large percentage of these babies had been given what was probably over-vigorous resuscitation. Furthermore, they had almost certain evidence that a few babies who would have recovered from the lesion which was blamed for their death, had been killed by extensive pulmonary emphysema which had come as a result of positive pressure resuscitation. In addition, the pædiatrician at the hospital, Dr. Stening, had told him that since they had very much curtailed resuscitation with oxygen under pressure, there were fewer babies being lost in the neonatal asphyxia group. He knew as well as anybody how very difficult it was to stand by and not force oxygen into a baby, in an attempt to inflate his lungs, when he was not showing signs of breathing within a few minutes. However, it probably was true that if the child would not respond to the conservative methods available, he probably was not going to survive in any case.

Dr. Macbeth added that there remained one more dangerous type and more useless type of resuscitation which was sometimes used. That was manual artificial respiration, by compressing and releasing the thoracic cage. If a child had not breathed, there was no resilience in the lung which would respond when pressure on the thoracic cage was released and the spring in the ribs would certainly not open the alveoli or draw in any appreciable quantity of air through the trachea. On the other hand, they had found that babies subjected to this treatment had been extensively damaged in the thorax and had even sustained a ruptured liver.

Dr. Macbeth then discussed chemical stimulants to respiration. He said that there were certain chemicals

which had a subconvulsant effect, when given in suitable doses, and which stimulated the chemoreceptors in the carotid sinus. The best known of those was lobeline. If a baby did not breathe within four or five minutes and the other methods such as sucking out the mucus and the intranasal administration of oxygen had been applied, most obstetricians considered that 0·25 millilitre of lobeline solution given intravenously had an excellent effect in stimulating a gasping type of respiration. He gave that into the umbilical vein and milked it towards the baby's body. He had very frequently found that within a few seconds the child responded and after a few gasps normal respiration commenced. The critics of this drug said that it was dangerous and caused convulsions which could be fatal. He himself had used lobeline on very many occasions and had never found a child to convulse with the dosage mentioned. Furthermore, he had written to Dr. Kate Campbell in Melbourne, whose experience of these things must be unique in Australia, and she, herself, used lobeline in very much the same way as he did.

Dr. Macbeth concluded by saying that the resuscitation of the newborn baby commenced during the conduct of the labour, and if a doctor was unfortunate to have delivered a child who was deeply asphyxiated, his advice was to treat him gently, to expect him to breathe after the use of the conservative methods which he had advocated, and not to lay upon him the extra burden of damage to his lungs or his viscera in an excess of enthusiasm or anxiety. If he would not respond to conservative treatment, he probably would not live after temporary revival by heroic attempts at blowing his lungs open.

DR. W. R. M. SHAW then read a paper in which he discussed the subject from the point of view of the anæsthetist.

DR. CLIFTON WALKER opened the discussion on behalf of the section of pædiatrics. He began by saying that emphasis had been placed on the best method of applying oxygen to the newborn baby and it had also been suggested that the infant should be placed with his head low and face turned to the side and await events—he would breathe or not. Oxygen administration did not replace the need for diagnosis. Many infants who were apnœic or in some respiratory distress did not need oxygen administration. A diagnosis of the cause of the respiratory insufficiency was the prime essential and then application of the specific treatment. An infant should not be cast aside and placed in the head low position if he had, for example, laryngeal atresia; he needed tracheotomy. Even so-called normal birth was a traumatic process, as 25% of newborn infants had blood in their cerebro-spinal fluid and about an equal number had retinal hæmorrhages. Cephalhæmatomata might cause so much blood loss that a transfusion of blood was essential. Clement Smith had summed up the situation in his article "The Valley of the Shadow of Birth".

Dr. Walker then said that prematurity was a major cause of respiratory difficulty and a lessening of its incidence would be welcomed by the pædiatrician. Heat loss was prevented by covering the newborn baby immediately after birth, but recent work was in progress in Scandinavia to try the effect of hypothermia. Also clamping of the cord was postponed to allow about a quarter of the infant's blood volume to come from the placenta. This latter method was not universally approved as some authorities thought that it might overload the circulation and actually lead to further respiratory distress. Post-maturity was also a hazard. Discoloured liquor amnii was generally thought to indicate fœtal distress, and as this sign was found predominantly in the post-mature infant it appeared reasonable to conclude that post-maturity was responsible for many cases of respiratory insufficiency at birth. The Aberdeen investigation a few years ago, in which induction of labour had been performed whenever a primigravida aged 25 years or more remained undelivered at 41 weeks gestation, had resulted in a considerable reduction in perinatal mortality.

Dr. Walker went on to say that amnesics, analgesics and anæsthetics were of great help to the mother but caused respiratory depression and should be used with discrimination. Intracranial hæmorrhage and œdema were potent factors in inducing respiratory difficulty, and it was important to realize that in many cases the bleeding was over the parietal lobe of the brain, was predominantly unilateral and could be dealt with by surgery. A tense fontanelle, inequality of the pupils, irritability and twitchings or convulsions were pathognomonic. A coronal subdural tap and the withdrawal of 10 millilitres of unclotted blood were likely to afford immediate relief and should be followed by craniotomy two or three days later. He feared that in the past too many of those babies had been treated medically instead of surgically. Lumbar puncture was not the procedure of choice, and in fact was contraindicated. The babies might show a striking pallor and in the differential diagnosis fœto-maternal transfusion must be considered. The infant might have lost blood behind the placenta or back into the mother's circulation. The pallor might be extreme, the condition might be diagnosed as asphyxia pallida and a grave prognosis given, whereas a transfusion of blood dramatically changed the situation. If the bleeding episode had been recent the hæmoglobin level might not have fallen, and it was not to be relied upon in deciding on the necessity for a transfusion. Large amounts of blood had been given; on one occasion Dr. Bruce Chown had used 390 millilitres. Another condition which caused marked respiratory distress was occlusion of the posterior nares. The inability to pass a catheter through the nares meant obstruction. An anæsthetist's airway placed in the mouth would help supply air for the infant until surgery could be arranged. The obstruction might be only a thick plug of mucus, and the routine passing of a catheter through the nares of the newborn baby was desirable. A marked recession of the mandible carrying the tongue back into the oropharynx occurred occasionally and might cause extreme respiratory distress. Such an infant did not need oxygen administration but simple positioning: he needed to be placed prone with head low and to the side. Constant supervision was essential. Rarely it might be necessary to stitch the tongue to the lower lip, but in none of his cases had this procedure been required.

Dr. Walker then referred to a rare but interesting condition, the duo syndrome of the laryngeal nerve. In the previous year he had seen a typical case. The baby had been born by the breech; the head had evidently been in lateral flexion *in utero* and this had distorted the relationship of the structures of the neck. The nipping of the recurrent laryngeal nerve between the cricoid and thyroid cartilages had caused a husky voice and some dyspnœa, while compression of the internal branch of the superior laryngeal nerve and its accompanying vessels had led to some difficulty in swallowing. That baby had also had mild facial paralysis and Erb's paralysis on the flexed side, and before leaving hospital showed a marked tumour of the sternocleidomastoid muscle. An interesting observation had been the large cavity in the neck immediately below the left mandible which exactly accommodated the shoulder.

Dr. Walker then said that tumours in the neck might cause respiratory distress through pressure on the trachea. Recently he had seen a newborn baby with an extremely large goitre, and the head had had to be kept in extension to prevent complete apnœa. That posture had enabled the infant to nurse at the breast and breathe freely. It had recovered in eight weeks. A point of interest was that the mother had been taking a mixture containing potassium iodide for chronic bronchitis throughout her pregnancy.

Dr. Walker went on to say that laryngeal anomalies, atresia, neoplasms, etc. might make tracheotomy necessary. Intragastric oxygen might keep the baby alive until surgery could be arranged. Dr. Edith Potter had stated "It has always seemed to me that gastric oxygen must be completely ineffective in oxygenating the blood". The superintendent at his hospital had used intragastric oxygen as a means of resuscitation in well over 100 cases and had been favourably impressed. Too vigorous pharyngeal suction at birth would sometimes cause œdema of the larynx with respiratory difficulty. Tracheo-œsophageal fistula should be diagnosed early because of the constant escape of mucus from the mouth. These infants should not be fed, and early surgery was indicated. An undeveloped epiglottis might cause similar symptoms. Diaphragmatic hernia came into the differential diagnosis and chest films would disclose the condition. Congenital lobar emphysema should be discovered by radiological examination as the X-ray picture was characteristic; in it the trabeculæ (the bronchi and vessels) were seen crossing the area of emphysema. Lobectomy might restore normal respiration. When the mother had been febrile or there had been an early rupture of the membranes, pneumonia contracted *in utero* must be considered, and in such cases antibiotics were indicated. There were many other causes of respiratory distress at birth such as congenital heart disease, double aortic arch, macroglossia, phrenic nerve paralysis, drugs such as reserpine having been administered to the mother, a baby born of a diabetic mother, any condition causing abdominal distension, and so on. Each of those required its appropriate treatment. It was frequently stated that the baby of a diabetic mother showed marked

œdema at birth. He had never been able to recognize any œdema in those infants.

Dr. Walker summed up by saying that if a diagnosis could be made there was the specific treatment to be applied, otherwise general measures must be adopted such as injection of lobeline, coramine etc., intragastric oxygen, Eve's rocking method, mouth to mouth breathing and so on. The doctor should choose the method in which he had confidence and which he had the ability to apply. In conclusion, he would suggest that it was only possible to make a selection from the many methods advocated and hope for the best.

DR. A. H. HODGE asked what percentage of post-mortem examinations in newborn children revealed congenital abnormalities. He also asked Dr. Shaw what one should do with the meddlesome midwife.

DR. M. S. ALEXANDER asked what was the best way to deal with the baby with the umbilical cord around his neck.

Dr. Macbeth, in reply, said that if the cord could not be unwound it should be cut. The child would lose the blood in the placenta and cord, but otherwise there was a real danger that the cord would tear or pull off the umbilicus.

Another speaker said that he thought it was important for a diagnosis to be made. He suggested that hypothermia might lead to respiratory depression.

DR. S. E. J. ROBERTSON pointed out the importance of distinguishing the exsanguinated baby from the baby with asphyxia pallida. They closely resembled one another; but since the exsanguinated baby responded readily to transfusion, it was important that its condition should be recognized. He also thought that blind aspiration of the pharynx was often performed too enthusiastically and could cause damage. He had performed laryngoscopy on numerous newborn infants with asphyxia pallida, or who had died with asphyxia pallida, and had yet to see one whose larynx had been obstructed by mucus.

Dr. Shaw, in reply to the question about the meddlesome midwife, said that it was his practice to keep hold of the babies so that the midwife could not get at them.

Dr. Macbeth said that when transfusion was given through the umbilical cord it was important to be careful of the quantity of blood given; the newborn child had only 300 to 400 cubic centimetres of blood altogether. He pointed out that cutting the umbilical cord before the fœtal heart pulsations had ceased might lead to a considerable loss of blood. He said that Dr. Walker's remark about subdural hæmatoma was very true. The condition could cause severe respiratory depression, and removal of the blood sometimes led to speedy recovery.

Medical Practice.

SECOND ANNUAL REPORT TO THE PRIME MINISTER BY THE NATIONAL RADIATION ADVISORY COMMITTEE, JULY, 1959.

THE following is the summary of findings taken from the Second Annual Report to the Prime Minister by the National Radiation Advisory Committee, July, 1959.

The Medical Use of Ionizing Radiation.

The hazards of ionizing radiation have been widely publicized, sometimes in a way that caused unnecessary alarm. As a result, there is a danger that individuals may come to harm through reluctance or refusal to undergo necessary X-ray examination. It is obvious that the use of X-radiation is essential to medical practice.

The Committee strongly supports efforts being made by many responsible authorities to reduce this source of radiation exposure to a minimum consistent with medical needs.

Mass miniature radiographic surveys for the control of tuberculosis should be continued with modern techniques and equipment.

Federal Control of the Use of Ionizing Radiation in Australia.

The increasing application of ionizing radiation in medicine and industry in Australia could be seriously hindered by a multiplicity of controlling authorities. The Committee recommends that the Commonwealth Government should seek the necessary powers to bring all uses of ionizing radiation in Australia under Federal legislative control as soon as possible.

Australian Laboratories for the Measurement of Low Levels of Radioactivity.

A laboratory facility for the measurement of low levels of radioactivity should be established in Australia, additional to that in existence in the Australian Atomic Energy Commission. Accordingly, the Commonwealth Department of Health should consider establishing a suitable facility within its X-ray and Radium Laboratory.

Atomic Weapon Tests in Australia.

The Committee has received all relevant data on fallout over Australia from these tests. Each test has been completed safely, with a negligible addition to the background radiation.

Global Fallout in Australia and its Biological Implications.

Australian Measurements: The Committee considers that the present programme for monitoring global fallout in Australia is adequate; it is comparable in scope with those carried out in the United Kingdom and United States. Comparison of Australian and overseas data indicates that fallout levels here are about one-fourth to one-third of those in the more densely populated regions of the northern hemisphere.

Possible Biological Consequences: At present, any biological damage caused by low levels of ionizing radiation cannot be computed with precision. In its report of August, 1958, the United Nations Scientific Committee on the Effects of Atomic Radiation adopted generally pessimistic assumptions in simplifying the assessment of biological damage from fallout. On these assumptions, estimates have been made in the present report to upper limits for possible biological consequences to the Australian population of present and future fallout from all nuclear weapon tests to date.

Leukæmia: A maximum of 1 additional case of leukæmia every 2½ years for the whole Australian population might occur as a result of fallout; this should be compared with the normal incidence of about 1250 cases in the same period. Less than 30 additional cases might occur for *all time*.

Bone Tumour: A *maximum* of 1 additional case of bone tumour every 5 to 10 years for the whole Australian population might occur as a result of fallout; this should be compared with the normal incidence of about 500 cases in the same period.

Major Genetic Consequences: The *total* increase which might occur over all future generations as a result of fallout would be between 0·2 and 7 per million of the population; this should be compared with the normal annual incidence of 140 to 600 per million of the population.

The Biological Implications of Fallout in the Light of Recent Developments: Recent scinetific research has shown that the simplifying assumptions used in estimating somatic and genetic hazards from fallout give values which almost certainly over-estimate the danger. It is emphasized that even the most pessimistic estimate corresponds to a risk which is insignificant in comparison with the normal hazards of life. Fallout from all weapon tests to date will contribute only a very small addition to the average natural background radiation to which human beings have always been exposed.

Obituary.

ANGUS McNEIL.

ANGUS MCNEIL, who died on February 3, 1959, as the result of an accident at his home some days previously, graduated in medicine from the University of Sydney in 1941. He served on the resident medical staff at the Balmain and District Hospital, Sydney, until 1942, when he joined the Australian Army Medical Corps. From August, 1942, to July, 1944, he was stationed in the Northern Territory, first at the camp hospital at Tennant Creek, and later at Banka Banka. Then he joined the 2/6 Field Ambulance in the Seventh Australian Division and remained with this unit until January, 1946; this period included the Borneo campaign, during part of

which Dr. McNeil was stationed at Balikpapan. In July, 1946, he was transferred to the reserve of officers.

Angus McNeil then commenced practice in Kempsey in partnership with Dr. William Quinn, working mainly as a surgeon. Dexterous in his surgery, he was popular with his patients, who liked particularly his cheerful disposition. In local public affairs in Kempsey, he always took an active interest. He was President of the Kempsey Sub-Branch of the Returned Sailors, Soldiers and Airmen's Imperial League of Australia for two years (1948-1949), and did much good work in getting assistance for distressed exservicemen during the flood of 1949. He showed a liking for medical administration when he became secretary of the Eastern District Medical Association, a position which he retained until he relinquished practice in Kempsey in 1956. His interest in local government was shown when he contested and won a by-election for a seat on the Kempsey Municipal Council in 1953, and in 1955 he was elected Mayor of Kempsey. Among his other interests was Legacy, and he was president of the Kempsey Contract Group for two years. He was also president of the local nurses' scholarship fund, a body which was responsible for giving one year's training in England to each of three nurses who graduated from the local district hospital. Dr. Quinn, who has supplied us with the information about Angus McNeil's career in Kempsey, has said that the thing that impressed him most about McNeil was his ability to meet and make friends with people from the top walks of life.

After leaving Kempsey, Angus McNeil took up the position of Assistant General Secretary of the Federal Council of the British Medical Association in Australia, to which he had been appointed in October, 1955. He commenced duty in February, 1957. His sudden death just two years later not only cut short a promising career, but deprived the medical profession of one who seemed set to serve his colleagues in a most effective way through the Association. The whole profession has mourned his passing and has felt and expressed sincere sympathy with his wife and children, in which we join.

DR. J. M. DWYER writes: Angus McNeil came to the Northern Territory in 1943 as a newly joined medical officer. His willingness and eagerness to get to work was almost embarrassing. He went first to take over 55 Camp Hospital at Tennant Creek, where shortage of accommodation made expansion imperative, and there were many other disabilities and deprivations besides. His ingenuity and initiative resulted in an improved design of ward, which became standard for 11 Line of Communication Subarea, which extended medically from Oodnadatta to Birdum and from Mount Isa to Hall's Creek. The design of the ward actually brought about a reduction of temperature internally of about 20° F. in the hot weather. From October to the end of March an avearge of one day out of three was over the century, and of course many were considerably above. Troops frequently found it impossible to find water cold enough to use for a shower. Some painful experiences occurred in raw troops passing through, as the ground temperatures of about 170° F. were transmitted to the water pipes. Later, at Banka Banka Angus had a rich experience in treating cases of heat exhaustion in personnel passing through by convoy on the very hot stage from Barrow Creek. It was not unusual to have half a dozen men with temperatures around 106° to 107° F. and often unconscious at the end of the stage from the south. They never developed signs on the journey south. It says much for the care and training of his orderlies that Angus never lost one of these patients. He and his O.C., Major Chequers, at "Banka" were tireless in conditions which were far from pleasant. The two were inseparable, and no task or journey was too hard for them to tackle. Their insuppressible cheerfulness was a constant morale booster. The "M.O. at Banka" became famous all along "the track" for his work, energy and sense of fun. He never seemed to run out of ingenious ideas for entertainment and betterment of the troops. He had fine qualities as an officer and leader.

DR. J. G. HUNTER writes: The news of the unexpected and tragic passing of Angus McNeil came as a great shock to all his friends and colleagues. Indeed it is difficult for those who were closely associated with him to realize that his energetic, bright and engaging personality is no longer with us. Others will tell of his services to the community generally and in particular to ex-service personnel and their dependants. It is my privilege to refer to the services which he so ably rendered to the Association. Soon after commencing practice in Kempsey he interested himself in the affairs of the Eastern District Medical Association, and in 1949 was appointed Honorary Secretary of that Association and also its delegate to the Annual Meeting of Delegates of Local Associations, positions which he occupied until 1956, when he retired from general practice to take up the post of Assistant General Secretary of the Federal Council. A good debater, with a keen sense of humour, his opinions always commanded respect at the annual delegates' meeting. His administrative training in civic affairs and his knowledge of the Association gained through his work on behalf of the Local Association eminently fitted him for an executive position in the Association. And so the Federal Council had no hesitation in appointing him as Assistant General Secretary in October, 1955, and regarded itself as fortunate in securing his services. He commenced his duties as Assistant General Secretary on February 4, 1957. In order to gain as wide a knowledge as possible of the working of the Association and the problems of the profession, he was a constant attendant at all meetings of the committees and of the Council of the New South Wales Branch and acted as Assistant Secretary of that Branch. He made it his business to study and inform himself of the needs and problems of the profession. For him the British Medical Association was the centre of his future existence, and his death is a great loss to the Association.

CHARLES AUGUST THELANDER.

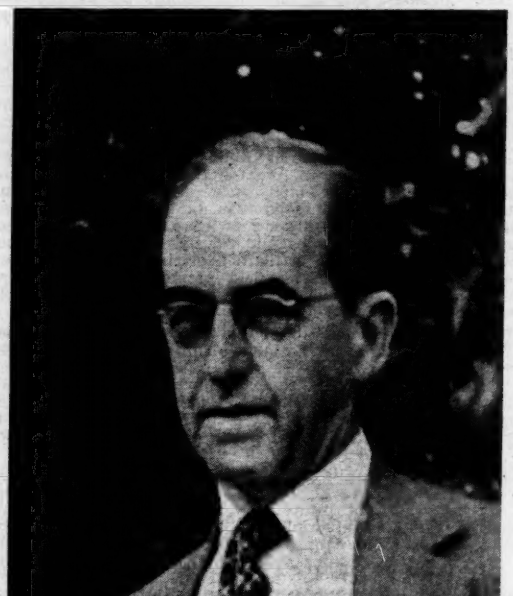
WE are indebted to Dr. Ernest Culpin for the following account of the career of the late Dr. Charles August Thelander.

The passing of Charles August Thelander has removed from the medical profession, after a long and distressing illness, another of those who were beloved by their patients and respected and esteemed by their fellow practitioners.

My first recollection of Thelander is when he came from the Toowoomba Grammar School to the Brisbane Grammar, where he followed me as school librarian, and he has always been prominent in my memory. I left the school to attend the University of Sydney; Thelander subsequently proceeded to the University of Edinburgh, where he had a very distinguished career as a medical student, taking his medical and surgical degrees in 1907. My next meeting with him was when he took over the practice of the late Dr. MacNamara in Stanley Street, East Brisbane, about 1911. I was then practising in conjunction with the late Dr. E. J. S. Spark in Vulture Street, South Brisbane. We met occasionally as general practitioners do, and at B.M.A. meetings, then held in the Y.M.C.A. Building in Edward Street. Thelander received a commission in the Australian Army Medical Corps, of which he was proud; but to his regret circumstances prevented his enlistment in the Australian Imperial Force for the 1914-1918 War, whereas I was more fortunate. Thelander subsequently moved to the house of the late Dr. Bancroft, at the corner of Wharf and Ann Streets, which is now an hotel. On returning from the war and commencing specialist practice, I secured rooms in Byrne Terrace, now a residential, but then being conducted by the wife of the late Dr. Hammond of Toowong and her sister, Miss Lowenthal, as professional rooms for medical practitioners, where several returned men obtained accommodation. Dr. Thelander, who then had a delightful home in Adelaide Street, Clayfield, also had his rooms there, where he practised as a specialist in diseases of women. Our rooms were on the upper floor and adjoining, and communicated by means of a balcony. It was here that I really came to know and appreciate the worth of Charlie Thelander, who was honorary surgeon at the Lady Lamington Women's Hospital, and subsequently at the Brisbane Hospital, which he served faithfully for years. It was there that our association led to the development of a project which became one of Charlie's great interests in life, and which under his unfailing efforts had considerable influence in helping the standard of medical practice in our community.

Many practitioners were looking for accommodation and security of tenure; we used to discuss ways and means. Two business acquaintances approached me with a definite proposition, including the purchase of a site for building and provision of finance. I introduced them to Dr. Thelander, who was possessed of considerable business acumen; a number of medical men were approached and a committee of five was appointed, including the late Dr. Russell. The proposed finance plan was dropped under the able leadership of Dr. Thelander, who brought forward and arranged for a much better system of finance. A (cooperative) company of medical men was formed, the necessary site was purchased and the late Lange Powell

was engaged for the architectural work. Thanks to Dr. Thelander, the name Ballow Chambers was adopted as a tribute to the memory of Dr. Ballow, who in the early days went as a volunteer to give medical aid in an outbreak of typhus in Moreton Bay, where he died from the disease. From the inception of the company, under the guidance of our leader, it was stressed that "Ballow" must encourage the highest ideals of professional skill and ethics. To help with this objective, much consideration was given to the Articles of Association. Ballow Chambers Limited was the first cooperative building effort of medical practitioners in Brisbane; its aim has always been to improve and encourage a high standard of medical practice. The building is an ornament to Wickham Terrace; it stands as a memorial to Dr. Ballow, who gave his life in the cause of duty; it should be an incentive to its



tenants to carry out the highest ideals of the medical profession. Ballow Chambers also stands as a memorial to Dr. Thelander, to whose efforts so much is owed by those who occupy its professional suites, and also by those who go there seeking relief from their troubles.

Charles was an idealist; his work had to be of the best—he realized that his patients required more than mere attention to physical ailments. He was a man of character and conviction. His adherence to chloroform as an anæsthetic was well known, as he knew how to use it. In discussions he was always courteous and ready to listen to the opinions of others, to which he gave careful consideration. His business acumen was also put to good purpose as a director of the Australian Provincial Assurance Association Ltd., which he served for many years, and which is well and favourably known to the British Medical Association in this country. His son, also Dr. Charlie Thelander, was one of the unfortunate victims of the *Centaur* tragedy.

DR. T. H. R. MATHEWSON writes: Dr. Charles A. Thelander was born in 1882 at Yangan in the south of Queensland, where his father was engaged in farming. After winning a State school scholarship at the local school, he attended Toowoomba Grammar School and, while there, secured first place in the junior examination of the University of Sydney. Later he attended the Brisbane Grammar School when the late Mr. Reginald Roe was headmaster. Although he subsequently secured one of the three scholarships entitling the holders to entrance to the University of Sydney, he decided to study medicine at Edinburgh, where he began his medical course in 1902. At Edinburgh he gained distinction in all his examinations, winning two important scholarships, one during his course and the other on graduating, when he was placed *proxime accessit* to the student placed first in the final examinations. After graduating he accepted the offer of the late Professor Greenfield to become his house physician, and later the offer of the late Professor Caird to become his house surgeon. After these appointments, Dr. Thelander attended clinics on the Continent.

Professor Greenfield, who occupied the chair of pathology in the University and was Professor of Clinical Medicine at the Edinburgh Royal Infirmary, invited Thelander to become one of his assistants in the department of pathology at the University. He was too interested in the practice of medicine, however, to be tempted by such an offer, and returned to Queensland. For a short time he acted as *locum tenens* for a doctor in Ipswich, and then he started practice in a house in Leichhardt Street, Brisbane. Shortly afterwards a vacancy occurred in East Brisbane, and there he established himself in general practice.

As a result of his diagnostic, therapeutic and operative skill and his sympathetic understanding of his patients, he built up a large practice. Although he was prepared to undertake any major surgical operation, he never did so without giving due consideration to the patient's welfare. He said that he sometimes saved patients from what he considered unnecessary surgical interference; but he was always quick to act in the case of an emergency. To quote an example: one night about midnight he received a message from a doctor in one of the outer suburbs that he was sending into hospital a patient suffering from an acute abdominal condition. Without waiting to be notified of the patient's admission, he proceeded to the hospital to await his arrival and have everything in readiness for the operation. During the operation (for the repair of a perforated gastric ulcer), earwigs and other insects which are attracted to a light on a summer's night darted to and fro, sometimes landing on the sterile towels. The patient made an uneventful recovery.

Dr. Thelander always had the courage of his convictions. He would operate on a patient in her home, if he considered that there was risk of cross infection in a hospital. He has performed a hysterectomy on a patient in her home, with excellent results. Those were the days when mothers were confined in their own homes and breast-fed their babies.

Dr. Thelander was an original thinker. He never slavishly followed traditional methods of teaching without examining their validity. He was frequently engaged in some form of research in the fields of clinical surgery and medicine, as well as in other fields. He devised new operative techniques. He was always able to improvise, and he was expert in making his own equipment, whether for carrying out some special investigation or for use in an operation. He was one of the first surgeons to have his patients ambulatory as early as possible after abdominal operations, when the accepted practice amongst his colleagues was to keep them in bed for three weeks after appendicectomy. Soon after commencing practice he was appointed honorary visiting surgeon to the Lady Lamington Hospital, and when the patients in this hospital were transferred to the Brisbane General Hospital, he was appointed honorary visiting gynæcologist to that hospital.

Although most of his time was occupied in caring for his patients, his interests were widespread. Even while he was a student in Edinburgh, he was actively associated with the work of the Australasian Club, of which he was president on several occasions.

Dr. Thelander was the prime mover in the formation of a company, whose aim it was to erect a building on Wickham Terrace to provide accommodation for doctors who wished to become shareholders in the company and at the same time procure security of tenure for themselves. Until comparatively recently he was chairman of directors of the company. The building, when erected, was named Ballow Chambers in memory of Dr. David Keith Ballow, who, while medical superintendent of the quarantine station at Dunwich, Moreton Bay, fell a victim to typhus fever and died on September 29, 1850.

Dr. Thelander was a member of a philosophical circle comprised of members of various professions and callings, which met in his rooms each month, when some lively discussions took place. He was always a keen debater. He was chief medical officer of the Australian Provincial Assurance Association Ltd. in Queensland, and also a director of the Association. He was always interested in the land and was a regular visitor to the Royal National agricultural shows, where he spent a good deal of his time viewing the livestock, especially the cattle.

He was a man who enjoyed the company of his many friends, and for years entertained them at his house on Saturday evenings. He had a subtle sense of humour. Gardening and bowling were his chief outdoor forms of recreation.

Dr. Thelander was married twice. By his first wife he had three sons, and by his second wife, who survives him, a daughter. The loss of his eldest son, Charles, who was a medical officer on the *Centaur* when she was torpedoed, caused him sorrow from which he never fully recovered.

About eight years ago he realized that he was developing the early signs and symptoms of paralysis agitans. In order to save his family anxiety, he refrained from telling them about his condition until they began to notice his disability. With characteristic courage and determination, he continued to carry on his work as long as it was physically possible, while submitting to all known forms of treatment which held out any prospect of staying the progress of the disease. Although he spent the last nine months of his life in hospital, to within a few days of his death he insisted on getting out of bed each day. Those who were privileged to know him mourn the loss of a friend of noble character.

DR. L. P. SAPSFORD writes: To a long line of house surgeons at the Brisbane Hospital, the late Dr. C. A. Thelander was a personality none will forget. In the pre-war years when resident medical officers were few, it fell to each man's lot to do a term with "Thely". Not only did one become his resident, but in turn one became his anæsthetist, and if it is possible to forget the former, it is certainly not possible to forget the latter. Having done his medical course in Edinburgh, Thelander never lost his love for chloroform, which he used skilfully in both surgery and obstetrics.

Junior as his anæsthetist might be, in all cases, long and short, chloroform was, with rare exceptions, the only anæsthetic used in Thelander's theatre. He assumed responsibility for it himself, and as much in vaginal as in abdominal operations he was aware at all times of the anæsthetic state of the patient, advising the man with the bottle when to drop a little more, when a little less.

It was, of course, obligatory never to lose one's concentration on the job, or to let one's little finger slip off the carotid artery. Thelander's paper on "Chloroform Anæsthesia: A Report on 3000 Cases" (MED. J. AUST., December 28, 1940) demonstrated the safety with which these anæsthetics were administered. As his assistant at operations, one acquired a great respect for the dexterity with which he removed organs or tumours from the depth of the pelvis, more by touch than by sight. His incisions were never large, and he was inclined to scoff at the surgeon who "thought only of his own convenience". Though this is controversial ground, one had to admit that, at least by Thelander, intricate manœuvres could be performed in very small spaces.

He was, at his best, a fast surgeon, and, partly by virtue of the quick anæsthesia possible with chloroform, frequently did five major operations in the morning's session. He was good to his residents, and when time allowed demonstrated steps of his operations that were often very original and unorthodox. He taught them the handling of instruments, and usually allowed them to perform some parts of the operation. He was even-tempered at all times, and was never ruffled in the theatre. Even on one occasion of extreme provocation, when a junior nurse spilt a basin of near-boiling water over his ankles, he did no more than jump from foot to foot exclaiming repeatedly: "Stone the crows! Stone the crows!"

Thelander had many ideas that were far ahead of their time. He had always encouraged early ambulation, especially in obstetrics, and he refused to allow a patient with white leg to be immobilized in sand-bags. He was radical in the management of septic abortion, insisting that better results were obtained by early evacuation of the uterus. This became and remained the policy of the hospital, though it has been less rigidly followed in recent years since the introduction of antibiotics. In obstetrics he had the patience of Job, and his personality gained for him the utmost confidence from his patients. He was widely known for his lifelong policy of what was formerly a taboo practice, the removal of the placenta by cord traction. An oft-quoted retort was typical of his wit. When asked what one should do if the cord broke, he said: "Throw it away—it's no good to you." He had a long experience in the handling of babies. His common-sense and his practical approach to the everyday problems of early motherhood threw into ridiculous relief the regimentation that was at one time taught in the child-welfare schools. He was one of those astute physicians who recognized in paint the source of the lead poisoning in children and the subsequent chronic nephritis so common in former years. A Thelander resident would never fail to observe the nail-biter during the course of a routine examination, and look the more closely for evidence of nephritis.

Thelander had a keen sense of humour, and his wit was proverbial; his sayings are still quoted. Even when his infirmity was well established he did not lose his sense of humour. With immobile mask-like facies he would look you in the eye and say: "I don't see the joke any more." On one occasion, after listening to a long tale of domestic woe, he comforted a patient by saying: "You know, it is woman's great misfortune that, if she marries at all, she has to marry a man." As a witness in a legal case arising out of a serious oversight by a colleague at operation, when he was asked by a barrister whether he did not consider this a shocking thing, he evaded the trap by turning to the judge and asking if he was obliged "to adjudicate on this man's adjectives".

Thelander must have learnt early in life that the majority of human ills are cured by nature. He had the patience and wisdom to listen to his patient's story without interruption, and to treat her successfully with little more than the words of reassurance and encouragement that were needed. This was one of the secrets of his success. Up until his later years he had an enormous practice, and his patients looked to him for treatment whatever the complaint. He was primarily a general practitioner, and though he became widely known as a gynæcologist and regarded himself as a surgeon "with a leaning to gynæcology", he continued to be the family doctor for a great number of his original patients—for in the days before specialization there was no field of medicine that found him uninformed, and scarcely any branch of surgery in which he did not actively participate.

He had no illusions about his own ability. He used to make the enigmatic remark about mankind that "the average was below the average". His confidence in himself was barely surpassed by that of his patients. Indeed, he undertook the responsibility of treating most of the members of his own family, including those nearest to him. Few, if any, of their operations, were performed by any other surgeon.

Thelander was universally loved and respected by the nursing staff of every hospital. His standing with his colleagues was not quite the same. Though highly respected for his outstanding ability, he was not always loved. He despised cant and humbug, and openly sneered at practices which he considered deserving of contempt. In his attitude toward mistakes, however, he was kindness itself, and if he laughed it was with the discomfited, not at him. His juniors he would take aside and would quietly point out to them the error of their ways.

As his junior partner, with interests very narrow in comparison with his, it became increasingly obvious to me as his enforced retirement was imminent that I could not continue to offer the same services to his patients, or hope to acquire the faith and affection which he commanded. He used to say that he might live to 100, and practise till he was 90. He loved and lived for his work, and it must have been a bitter disappointment for him, as it was for many an old patient, when it was realized that he would not be able to continue. Throughout his prolonged invalidism, with the ever-increasing restriction of his mobility, he uttered no words of complaint and awaited his time with stoic fortitude. To those of us who profited most from his teaching, his help and his encouragement, his unique personality will remain a memorable and vivid thing, his precept and example a guide to us always.

Correspondence.

TOBACCO SMOKING AND LUNG CANCER.

SIR: Dr. K. W. Starr, in his letter of August 8, 1959 states that statistics were never intended to show a causal relationship. The term statistics is used in two senses. In common parlance it is generally used synonymously with numerical data. "Statistics" also refers to the statistical principles and methods which have been developed for handling numerical data. Statistics in this sense is a scientific method which has become an indispensible tool for the research worker. In various scientific fields, statistics (in the latter sense) assists in determining causal relationships.

As in the animal experiment, so in the human investigation, statistics are used as part of the scientific method. The difference is not in the statistics, but in the material to which the statistics are applied. For this reason, it is unwise to label the investigations of lung cancer as "statistical" without due qualification. Basically, the investigations into lung cancer have been of the epidemiological type (Fowler, 1955). The epidemiological investigation may be similar to the animal experiment in that a group of individuals is compared with a group of matched controls. It differs from the animal experiment, and for that matter, from the clinical investigation of the effectiveness of a drug, by the fact that the experimental group is selected by the possession of the characteristic to be investigated. This has a definite disadvantage, as it remains uncertain whether or not the individuals with the chosen characteristic will vary from the population in other ways. For this reason, the epidemiological (not the statistical) investigation cannot prove a causal relationship with the apparent finality of the animal experiment. The problem can be partly overcome by examining the groups for other likely influences and eliminating these as significant factors. When this is done, an epidemiological investigation may provide evidence to support causal relationship. It may not be possible to provide further experimental proof of a given causal relationship, as the results of animal experimentation are unreliable indications of the operation of causal relationships in man.

In the case of smoking and lung cancer, the most definitive of the investigations are of the prospective type (Doll and Hill, 1956, and Hammond and Horn, 1958). A large group of individuals was questioned by circular as to whether or not they smoked, in what form, how long, and so forth. Then the death of any individual of the group has been ascertained, and the death rates from cancer of the lung of the various classes of smokers have been computed and compared. Both studies have shown a highly significant excess of deaths from lung cancer amongst smokers. Moreover, there was a regular progressive increase of death rate from cancer of the lung corresponding to a progressive increase of the amount smoked. There was some increase in deaths from other causes, including coronary heart disease, and other respiratory conditions. The probability that these latter differences were due to chance was much greater than for cancer of the lung, and their significance is a little uncertain. However, Berkson (1959) has suggested, amongst other things, that it is possible that smoking increases the general mortality rate by exerting an aging effect. However, in view of the lack of statistical significance for much of the increased mortality rate, it would be unwise to accept this argument at present.

Although Stocks and others have suggested the presence of an "urban factor" additional to smoking, Stocks's (1957) investigation of the influence of smoking is consistent with the findings of other workers. Although the correlation between tobacco consumption and lung cancer incidence is not exact, Doll and others (1959) have shown that there is a distinct relationship in 16 countries, U.S.A. and Japan providing the chief exceptions. As discussed by Hammond (1959) and Doll and others (1959), there are several possible explanations of the exceptions. In the U.S.A. one factor has been that cigarettes are discarded with a larger butt than in England. It would be unwise to disregard the evidence in favour of the effect of smoking, because of these exceptions. Dr. Starr mentions immunity of non-European races despite heavy cigarette smoking. I have been unable to find reliable age-corrected rates to confirm this claim.

Whether or not the habit of inhaling is related to lung cancer incidence is uncertain. Schwartz and Denoix (1957) have presented evidence that suggests that it is.

Fisher (1958) has suggested that people who smoke have a genetic make-up which predisposes them to both smoking and lung cancer. This hypothesis does not account for the very great increase of lung cancer, which, it is generally agreed, is real and not apparent. Moreover, there is evidence that persons who change from being heavy smokers to non-smokers, reduce the likelihood of developing lung cancer.

Taken on its merits, the evidence shows that cigarette smoking is likely to cause lung cancer. There is also evidence that smoking is not the only cause. The evidence may not be final, nevertheless it is sufficiently impressive to take preventive measures by avoiding and advocating the avoidance of a probable carcinogen.

Dr. Starr suggests that if the incidence of lung cancer is reduced, the population may develop other cancers instead. There is no evidence for this, and in fact, the age-corrected male mortality rates show that mortality from all cancers is still rising in the U.K. and U.S.A. This is due largely, if not entirely, to the continued rise in lung cancer (Hammond, 1958).

Dr. Starr infers that the campaign against smoking has failed. It seems rather that the campaign has yet to start. "Experience has shown that when the public conscience has become thoroughly aroused about . . . a particular death rate . . . that death rate has tended to come down whether or not the [precise] pathology was properly understood" (Stocks, 1953).

In dealing with an addiction, rationalization is a formidable obstacle, which is overtly encouraged by the widespread advertising of tobacco products, and by the ready publication of any views dissenting against smoking as a cause of lung cancer.

Yours, etc.,

243 Waterdale Road,
Ivanhoe, Victoria.
August 16, 1959.

ALASTAIR H. CAMPBELL.

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CANCER, A DISEASE OF THE NERVOUS SYSTEM.

SIR: It was with great interest that I read Dr. Haslett Frazer's thoughtful letter (MED. J. AUST., July 25, 1959) on the current correspondence under the heading of "Cancer, a Disease of the Nervous System".

I feel grateful to Dr. Frazer for reviving interest in what I had long felt to be a forgotten hypothesis.

It is stimulating to realize, that, after twenty-six years, someone has remembered that, so long ago, I put forward the idea that cancer might be a psychosomatic disease.

Dr. Frazer was commenting on a letter by Dr. Llewellin Davey (MED. J. AUST., May 30, 1959). I am most interested in the views of both Dr. Davey and Dr. Frazer, for they largely coincide with and supplement my own thoughts in May, 1933, published in *The Journal of the Cancer Research Committee of the University of Sydney.*

I am also very interested in the views expressed by Mr. Kenneth Starr (MED. J. AUST., August 8, 1959) in his letter under the heading of "Tobacco Smoking and Lung Cancer".

Mr. Starr contends, and I agree with him, that statistics, despite their obvious value in various other ways, have often been used to show a causal relationship—a role for which they were never intended.

Mr. Starr goes on to say that, on the basis of statistics, to avoid lung cancer, smokers should either live in the country or change their sex. It would be easy to make a frivolous reply to this, but I am not frivolous about the frightful and frightening problem of neoplasia. We have all seen our patients and our friends and our loved ones die from this most desperate of all diseases.

The matter is of such vast importance that I make no apology for my egotism in re-expressing my own views. As far as I know, I was the first person, with regard to the problem of cancer, to suggest the possibility of a

jump from the psychological to the biological, from the Psyche to the Soma.

The validity of my 1933 opinions is, to some extent, substantiated by the later discovery of the beneficial influence of female hormones in cases of prostatic carcinoma.

To Dr. Frazer, Dr. Davey and Mr. Starr, I extend my admiration for their disregard of orthodoxy. Whether or not anyone extends any admiration to me, does not matter. All that matters is the answer to the questions of why some people contract cancer and why some do not, and if any of the four of us can contribute something towards the solution of this mounting problem, we shall not have lived in vain.

I will submit a paper to you, Sir, in which I will put in detail the views of Dr. Davey and Dr. Frazer, as well as mine.

If Mr. Starr will forgive a kindly-meant pun, I would like to quote the words of a man who had a much greater intellect than I possess.

"Our faults are not in our stars, but in ourselves."

It is time, in my opinion, that those who possess the requisite intellect, should explore the possibility that cancer may be a psychosomatic disease.

It is the only unexplored avenue.

Yours, etc.,

135 Macquarie Street, ARTHUR D'OMBRAIN.
Sydney, N.S.W.
August 16, 1959.

AN APPEAL FOR MICROSCOPES.

SIR: May I through your columns appeal to doctors who have no further need of their microscopes to give them to the Christian Medical College and Hospital, Vellore, South India.

The Vellore Christian Medical College and Hospital is a medical training centre affiliated with Madras University, and in addition to treating 180,000 out-patients per year, has 800 beds for in-patients. It has 300 students studying for the M.B., B.S. degree, as well as about 20 post-graduates working for the M.D. or M.S. degree. Microscopes are urgently needed for the teaching programme.

Australian doctors who have no further need for microscopes which they may have bought as medical students, may be willing to give them to Vellore. The college and hospital has international and interdenominational backing from 40 churches and missions throughout the world, and is worthy of support.

I will be personally responsible for collecting the microscopes and shipping them to Vellore.

Yours, etc.,

Hon. Secretary, R. L. WALKER.
Australian Board of the Vellore
Christian Medical Centre,
193 Macquarie Street,
Sydney.
August 12, 1959.

HEAD LICE CURE FOR *INFECTIOUS HEPATITIS*.

SIR: Recently a patient asked me how the doctors were getting on with the then infectious hepatitis epidemic. I said treatment was difficult, but some progress had been made. He said "Have you tried the head lice cure yet?" I replied that progress had not got that far. He replied, "Well you're wasting your time unless you do", and then produced the attached excerpt, the accuracy of which I am unable to verify.

Excerpt from "Journey to the Far Pacific", by Thomas E. Dewey, page 255.

> A Dutch doctor tells of a number of cases of Jaundice that came to his attention. He prescribed the only known treatment, rest and a good diet, under which it usually takes about six weeks to recover if the patient follows the doctor's orders. To the doctor's astonishment, several of his patients came back cured in three or four days. Inquiry revealed that they had gone home and followed the local custom of eating Head Lice.
>
> Profoundly impressed by this unknown cure for a baffling disease, the doctor had lice gathered from the heads of workers in a near-by compound, put them in capsules and tried to persuade some of his other patients to try the remedy. The first one willing to try it was an American, who was cured in three days; nobody knows why. Now the doctor has launched a research project to find the secret of the cure. I was not sure myself whether I would rather have jaundice or eat the lice. But after all, this cure is no more repulsive than pus from a sick cow which we use to prevent smallpox.

Yours, etc.,

55 New South Head Road, BERTRAND A. COOK.
Vaucluse.
August 14, 1959.

ON ANEURYSMS.

SIR: Your leading article of August 1, 1959, follows up the article by John Loewenthal, G. W. Milton, and G. V. Shead, with discussion of diagnosis and treatment of leaking abdominal-aortic aneurysm.

In my personal experience of some seven cases of this condition operated on at the Royal Prince Alfred Hospital between July, 1955, and August, 1958, there were two survivors. The first one was reported in the MEDICAL JOURNAL OF AUSTRALIA of February 8, 1958, on page 183.

Improvement in the progress of this condition appears to me to be dependent on the following factors: (i) Appreciation by the medical profession that this is a curable condition. (ii) Early transport to hospital. (iii) Rapid transportation from admission department direct to operating theatres, without useless delay in attempts to resuscitate in the ward. (iv) Swift and deliberate surgery. (v) Meticulous post-operative attention to fluid and electrolyte balance and aseptic intravenous therapy. (One of the above cases died 14 days post-operatively from staphylococcal septicæmia secondary to his intravenous therapy for anuria and paralytic ileus which lasted 10 days.)

Yours, etc.,

A. F. GRANT.

Royal Prince Alfred Hospital Medical Centre,
Newtown.
August 13, 1959.

SOME OBSERVATIONS ON INGUINAL HERNIA IN THE ADULT.

SIR: Mr. T. F. Rose in his article on inguinal hernia in the adult (MED. J. AUST., June 6, 1959) advocates in most cases the use of the Bassini repair, but makes no recommendations as to the type of suture to be employed. In this connexion the work of Doran and Lonsdale[1] would appear to be relevant. By using silver clips applied to both inguinal ligament and conjoined tendon, they were able by radiological means to demonstrate separation of these two structures in eight of 13 cases six months after operation when absorbable suture material was used. Separation of the markers was by no means synonymous with recurrence; but if the Bassini repair has as a secondary aim the prophylaxis of direct herniation, then the use of non-absorbable suture material is mandatory. In a personal series of over 700 cases I have used successively stainless steel wire, braided tantalum and braided nylon, and found the last-mentioned suture material to be by far the most satisfactory. The stainless steel wire is stiff, difficult to work with and the ends a possible cause of pain even when carefully turned in. Subsequent X-rays of some of these cases showed that, despite the greatest care to avoid kinkage at operation, fragmentation had taken place. Braided tantalum, because of its high cost, was used as a continuous suture material. This prevents its spontaneous extrusion in the event of sepsis.

Obviously the conjoined tendon must be approximated to the inguinal ligament without tension, or atrophy of the former structure will result with consequent direct herniation, as Mr. Rose points out. Mr. Rose rather condemns the Tanner relaxing incision on the grounds that serious damage may be inflicted on the abdominal wall. Provided the incision does not extend beyond the edge of the rectus muscle, this fear appears to be without foundation. I find it frequently difficult to bring down

[1] *Brit. J. Surg.*, 1949, 36: 339.

the conjoined tendon without tension unless this manœuvre is employed, and have no hesitation in resorting to it.

Mr. Sidey (MED. J. AUST., July 18, 1959) advocates turning back a flap of rectus sheath to reinforce the posterior wall of the inguinal canal. It is apparent that in his hands this operation has proved eminently satisfactory; but in a personal experience of 30 cases of this procedure two direct recurrences occurred between the edge of the rectus muscle and the flap.

Mr. Rose rather dismisses the repair of the fascia transversalis as of little moment. Whilst paying lip-service to the technique of suturing the fascia transversalis on the medial aspect of the cord, I agree that it is of dubious value. Of far more importance is the insertion of one or two sutures lateral to the cord, as advocated by Bassini nearly 70 years ago. Great care must be taken to avoid undue constriction of the cord, or a swollen testicle or even a hydrocele may result.

In dealing with large or recurrent herniæ, the fascia lata grafting operation introduced by Gallie is a most satisfactory repair, but is now obsolete. In a personal experience of over 50 fascia lata hernioplasties, most patients developed a muscle hernia in the thigh, but in no case did it produce pain or disability.

Mr. Rose does not appear to favour the use of "implants", stating that they are liable to be followed by continuous pain, local tenderness and sometimes a limp. To date I have used stainless steel gauze on 21 occasions to repair difficult and complicated inguinal herniæ without any of the undesirable effects Mr. Rose mentions, no sepsis and no recurrences so far. Other prosthetic materials may prove more suitable, particularly nylon mesh. It would be rash and quite unjustifiable to use an "implant" where simpler methods of repair are adequate. Infection is the real hazard, and would necessitate removal of the "implant". In this connexion it is relevant to point out the serious infection in any repair is very apt to be followed by recurrence. Grace and Johnson[1] found a 40% incidence of recurrence after deep sepsis.

I thoroughly agree with Mr. Sidey that hernia repair should never be considered minor surgery. It is well to realize that the best chance of cure is at the original operation. Fallis[2] may have overstated the case when he declared "the real cause of recurrence lies in a technical error at the primary operation", but there is more than a little truth in the comment. With improved methods and suture materials, modern surgery should certainly have a lower recurrence rate than that of 12% quoted by Max Page[3] in 1943 in the experiment on London policemen.

Yours, etc.,

W. H. NEILD.

1 Union Street,
Newcastle, N.S.W.
August 4, 1959.

SECOND THOUGHTS ON HUMAN CANCER.

SIR: On Wednesday, August 19, 1959, Dr. K. W. Starr, the Honorary Director of The New South Wales State Cancer Council's Special Unit for Investigation and Treatment of Cancer, was invited by the Council of the Royal Australasian College of Surgeons to deliver the evening scientific address on "Second Thoughts in Human Cancer". Apparently uninvited newspaper reporters were in the audience, with the result that considerable radio and Press publicity was given to the subject of the lecture. For the most part this publicity was incorrect, misleading and sensationalistic.

It is to be deplored that a scientific programme into one of the greatest biological problems of today (namely, human cancer), costing a considerable amount of money and the concentrated efforts of approximately fifty trained workers, should have resulted in its use by the Milk Board for advertising purposes.

It is desired to inform the medical profession, which has been so cooperative in its support of this research unit, that if and when any work carried out at the Special Unit will improve the management or prospects of their cancerous patients, they will be the first to know. Further, the limitations and advantages of anything which is so proposed will be fully canvassed in accordance with proper professional conduct.

I wish to state also that, if the lecture is accepted for publication, it is hoped sufficient reports will be available for distribution through professional channels, so that doctors in New South Wales who could not attend the lecture will be able to inform themselves of what has happened, and to examine our experience with their usual critical appraisal.

Yours, etc.,

ALAN B. LILLEY,
Medical Director.

The New South Wales State Cancer Council,
The Basement,
Treasury Building,
Bridge Street,
Sydney.
August 31, 1959.

[1] *Ann. Surg.*, 1937, 106: 347.
[2] *Ann. Surg.*, 1938, 107: 572.
[3] *Brit. J. Surg.*, 1943, 31: 172.

ELECTRO-CONVULSIVE THERAPY AND INTRAVENOUS ANÆSTHESIA.

SIR: Dr. S. V. Marshall's letter regarding electro-convulsant-therapy and intravenous anæsthesia (MED. J. AUST., August 15, 1959) is, I am afraid, a classical example of the tendency of some anæsthetists to inflate relatively simple procedures into hazardous undertakings. What Dr. Marshall seems to forget is that many psychiatrists have by now accumulated greater experience of this procedure than most anæsthetists. In my own case, I have carried out the procedure single-handed (always using "Pentothal" and "Scoline") on more than 6000 occasions during the last six and a half years, without a single mishap. I feel sure there are many psychiatrists throughout Australia who have had even more experience. For how many years and for how many thousand times must a treatment be carried out safely before it can be regarded as safe?

Dr. B. J. Pollard infers (MED. J. AUST., June 27, 1959) that financial considerations are largely responsible for the psychiatrist's decision to carry out the procedure single-handed. How then does he account for the fact that so many psychiatrists in State departments are quite happy to work single-handed, even though by doing so they do not add one penny to their income?

The fact is that given ordinary competence and care (and obviously no therapy should be attempted without those essentials), the performance of the treatment single-handed is completely safe. The presence of a second doctor is, in the vast majority of cases, quite superfluous and carries with it, only too often, the very practical disadvantage that the patient does not receive treatment when he most needs it, but when it is possible for two doctors to be present at an arranged time. There are, of course, the very small minority of cases where, owing to some severe physical condition such as coronary disease, etc., the psychiatrist may wish a second doctor to be present. Even in these cases, I have never seen the second man carry out any procedure which a solo therapist could not have handled readily.

The opinion expressed by the Federal Council of the British Medical Association (MED. J. AUST., May 16, 1959) and the amendment to the Commonwealth Medical Benefits Scheme, to which Dr. Marshall refers, are very sensible acknowledgements of the above facts, and the withdrawal which he suggests would be a most retrograde step.

I hope that psychiatrists will not be deterred by the bogies with which Dr. Marshall attempts to surround a straightforward procedure, but will strive to make themselves ever more competent in this very necessary treatment.

Yours, etc.,

F. G. PRENDERGAST.

"Martalup",
254 St. George's Terrace,
Perth.
August 25, 1959.

SIR: It appears that another border clash has flared on the anæsthetist-psychiatrist frontier. This time Dr. S. V. Marshall (MED. J. AUST., August 15, 1959, page 230), in questioning the Federal Council opinion that it is good practice for a psychiatrist to give E.C.T. and the associated anæsthetic single-handed, avers that this is startling, and a ruling "contrary to established custom, ordinary prudence and common sense"—fighting words these, Sir—but let us attempt to be factual rather than emotional in rebuttal.

Dr. Marhsall's opinion of psychiatrists' ordinary prudence and common sense is apparently very poor; it would be profitless to pursue this point. However, I do wish to combat his assertion that "single-handed" E.C.T. is contrary to established custom. This is the reverse of the truth.

At the Receiving House, Royal Park, in the year from July 1, 1958, till June 30, 1959, over 6000 E.C.T.'s were given, all with relaxant ("Brevidil E") and many with pentothal, 100 to 250 mg., as well. A proportion of the patients were debilitated, aged, or had a history of recent or remote myocardial impairment. Amongst all these there were no untoward results. The longest "Brevidil" apnœa was 3 to 4 minutes, easily controlled with breathing-bag, mask and oxygen cylinder. All treatments were given "single-handed", i.e., by one doctor and the ward nursing staff.

The truth is, as Dr. Bignold points out on the same page of the Journal, that "the objection is, in effect, to minor anæsthesia being administered by a doctor who is not a specialist anæsthetist". This is an unreasonable and impractical attitude. E.C.T. is not a difficult technique, and the psychiatrist knows perfectly well from his own experience that it can be given safely and efficiently in the way that Dr. Marshall so vehemently deplores.

Yours, etc.,
J. F. J. CADE,
Psychiatrist Superintendent.

Receiving House,
Royal Park, N.2.
Victoria.
August 25, 1959.

FITNESS OF DRIVERS OF PUBLIC SERVICE VEHICLES.

SIR: The statement by The Royal Australasian College of Physicians on standards of fitness of drivers of public service vehicles, published in your issue of July 4, was framed specifically for drivers of buses and trams, at the request of the Department of Government Transport, New South Wales.

Dr. J. C. Lane, in his letter published in your issue of August 8, has properly drawn attention to an error in the article. The phrase "blood pressures above average normal figures" in each instance should have read "average blood pressures above normal figures"—the average blood pressure being defined in paragraph 5, in the section on hypertension.

The difficulty in defining normal blood pressure is fully recognized and the figures given in paragraph 5 were submitted as a guide, to be applied only to the initial medical examination of driver applicants. The World Health Organization has made similar recommendations in this regard.

The final paragraph of Dr. Lane's letter appears to be very much in accord with the general tenor of the statement.

Yours, etc.,
H. MAYNARD RENNIE.
Honorary Secretary,
The Royal Australasian College of Physicians,
145 Macquarie Street,
Sydney.
August 20, 1959.

A SURVEY OF ALCOHOLISM.

SIR: I would appreciate if you would publish in your Journal the following comments.

I read with great interest and considerable alarm figures published by Dr. I. R. Mackay in his survey of alcoholism (MED. J. AUST., 1959, 2: 176). According to his figures, 56% of car drivers injured in car accidents showed a positive blood alcohol test; similarly, drivers killed in road accidents (26%) and pedestrians injured in car accidents (45%). In all these cases the level of alcohol in blood was above 0·1%.

These figures are, of course, frightening, and one wonders why they were so much lower in my study on psychological aspects of car accidents (MED. J. AUST., 1958, 2: 282). The explanation of this discrepancy was already given by Dr. E. H. Derrick (MED. J. AUST., 1958, 2: 468): the number of car accident victims under influence of alcohol is much greater than it appears. The police hesitate to attribute an accident to alcoholic intoxication, unless there is a pronounced clinical picture of such an intoxication. But people are very well able to conceal such a sign, and even doctors are frequently not able to make a better assessment than laymen. If there is a scientific method, which would help to disclose in an objective way alcohol intoxication, where it is not detectable clinically, it should be used to its full extent.

There are no reasons why the community should not have the right to protect itself, even if the individual will suffer to the extent of a needle prick and of the loss of a small amount of blood (this blood anyhow regenerates in minutes or hours). Individuals suffer much more all through their life by severe restrictions imposed on them by society. Some of the restrictions are so severe that they lead to neurotic reactions, or to other psychological and behavioural disorders in adolescents and adults, and still society lets them suffer for the benefit of others. I advocate, therefore, compulsory blood tests for certain types of drivers. Drivers who were involved in accidents may become culpable and have no manifest signs of alcohol intoxication. For all other drivers the blood tests should be voluntary.

That brings up the question of prevention. Wouldn't it be better to do something about drunken drivers before they lie drunken and wounded on the road, and their car, passengers and pedestrians around them? The prevention is a very serious matter, and one which could be handled on the level of a Drivers' Guidance Council. Such a Council would deal with the personality of accident-prone drivers and among others with drivers accident-prone because of alcoholism. There is no doubt that alcoholism is a neurosis or a personality disorder, and therefore should be treated as such. And the people who should deal with the problem are psychiatrists, clergymen, psychologists and social workers. They should staff Drivers' Guidance Councils, similarly as Marriage Guidance Councils are staffed, and judges would know where to send offenders for rehabilitation. But also offenders themselves could seek help on a voluntary basis.

To sum up: compulsory blood alcohol tests for detection and voluntary Drivers' Guidance Councils for prevention and treatment.

Yours, etc.,
I. A. LISIWAN.

"Labrador",
217 Macquarie Street,
Sydney.
August 20, 1959.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

THE following extracts from *Hansard* relate to the proceedings of the House of Representatives on August 18, 1959.

Lung Cancer.

MR. WHITLAM asked the Minister for Health, upon notice—

1. When did the Government set up, pursuant to the resolution of the National Health and Medical Research Council in May, 1957, a body representing his department, the Department of Primary Industry, the Commonwealth Scientific and Industrial Research Organization and the tobacco industry to inquire into, and make recommendations upon, measures to reduce the risk of lung cancer confronting tobacco smokers?
2. When has this body met?
3. What recommendations has it made?
4. When did it make them?
5. What action he has taken on them?
6. When did he take this action?

DR. DONALD CAMERON: The answer to the honorable member's questions is as follows:

1, 2, 3, 4, 5 and 6. On 3rd September, 1957, at my invitation, an exploratory meeting was attended by representatives of the Australian National University, the Commonwealth Scientific and Industrial Research Organization, the tobacco industry and the Commonwealth Departments of Primary Industry and Health. It was decided that the Commonwealth Department of Health should investigate the possibilities of a detailed statistical investigation to ascertain the incidence of bronchogenic carcinoma under different environmental conditions in Australia. This statistical study has been undertaken but is not yet complete. As part of this study provision has been made for the financing by the Commonwealth of certain patho-

logical research to be undertaken by the Australian College of Pathologists into the influence of tobacco smoking on lung cancer.

Medical Benefits Scheme.

MR. WHITLAM asked the Minister for Health, upon notice—

1. How many claims were (a) accepted and (b) rejected by registered medical benefits funds during 1958?
2. What percentage of the cost of medical services for which claims were accepted was met by (a) the funds, (b) the Commonwealth and (c) the contributors?
3. What were the principal reasons for rejecting claims and what percentage of claims was rejected for each of these reasons?

DR. DONALD CAMERON: The answers to the honorable member's questions are as follows:

1. Statistics according to claims are not kept, but figures are available on the basis of individual services. In 1958 claims were accepted in respect of 15,962,140 individual professional services. Of these 461,323 did not attract fund benefit.
2. (a) 34·4 per cent, (b) 28·6 per cent, (c) 37 per cent.
3. The principal reasons for rejecting fund benefit were—(a) service during the waiting period (normally the first two months of membership)—0·77 per cent of services; (b) the illness was in evidence at time of joining—1·11 per cent of services; (c) maximum annual fund benefits previously paid—0·48 per cent of services; (d) optional services (i.e. services for which the member had not insured himself)—0·16 per cent of services.

Employment of Physically Handicapped Persons.

MR. FORBES: I ask a question of the Minister for Labour and National Service. I refer to his recent timely exhortation to employers to employ, wherever possible, physically handicapped persons who seek to rehabilitate themselves. Can the Minister indicate whether, and if so to what extent, the Commonwealth Government has set an example to private employers by itself employing such people?

MR. MCMAHON: The Government hopes that all people who can employ physically handicapped persons will do so in appropriate circumstances. So far as the Commonwealth is concerned, it is a matter for each individual department to decide how many physically handicapped people will be employed, and in what classifications. My department does make opportunities available for the employment of physically handicapped people, and certainly the Department of Social Services, if I may speak for my colleagues, goes out of its way to see that physically handicapped people are employed.

I might I think add that the Boyer Committee, which recently reported on the Public Service, did make some recommendations as to the way in which physically handicapped people should be employed in the Commonwealth Public Service. The report is now being examined within the departments concerned and, as soon as the relevant portions come to hand, I expect the Prime Minister will make it available.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Post-Graduate Training in Cardiovascular Diseases.

THE Post-Graduate Committee in Medicine, in conjunction with the Post-Graduate Medical Foundation, announces its intention to introduce a running course in cardiovascular diseases. This will comprise a series of evening seminars dealing with various aspects of the subject suitable both for general practitioners and for post-graduates studying for higher degrees or diplomas.

The first of the series will consist of seminars on hypertension under the supervision of Dr. G. E. Bauer, and will be held in the Maitland Lecture Hall, Sydney Hospital, from 8.00 p.m. to 10.00 p.m. as follows:

Wednesday, October 7: 8.00 p.m., "Normal and Abnormal Blood Pressure", Dr. H. M. Whyte; 8.30 p.m., "Blood Pressure and Heredity", Dr. R. B. Blacket; 9.00 p.m., "Blood Pressure and Pregnancy", Dr. Richmond Jeremy.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 8, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	1	3(2)	5(1)	..	..	..	..	..	9
Amœbiasis	..	..	..	..	1(1)	..	..	..	1
Ancylostomiasis	..	..	2	..	..	..	7	..	9
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1	..	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	2(2)	..	..	..	..	..	..	2
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1(1)	9(9)	..	..	1(1)	..	..	2	13
Diphtheria	..	..	..	..	5(5)	..	1	..	6
Dysentery (Bacillary)	..	..	..	..	7(4)	..	..	..	7
Encephalitis	..	1(1)	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	37(14)	34(13)	14(1)	15(11)	1(1)	..	..	..	101
Lead Poisoning	..	..	1(1)	..	..	..	..	..	1
Leprosy	..	..	..	..	..	..	2	..	2
Leptospirosis	..	..	5(1)	..	..	..	..	..	5
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	4(3)	..	..	..	..	..	..	..	4
Ophthalmia	..	..	..	..	..	..	..	9	9
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	1	..	..	..	..	..	1
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	17(10)	..	..	1(1)	..	..	..	18
Salmonella Infection	..	..	..	1(1)	..	..	..	..	1
Scarlet Fever	7(6)	10(7)	2(2)	9(6)	1(1)	2(2)	..	..	31
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	1(1)	..	..	..	1
Trachoma	..	..	..	..	2(1)	..	17	..	19
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	17(9)	20(13)	15(6)	4(4)	9(4)	5(1)	1	..	71
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Wednesday, October 14: 8.00 p.m., "Malignant Hypertension", Dr. James Isbister; 8.30 p.m., "Renal Hypertension", Dr. Ralph Reader; 9.00 p.m., "Modern Investigations", Dr. W. A. Seldon.

Wednesday, October 21: 8.00 p.m., "Blood Pressure and the Heart", Dr. J. G. Richards; 8.30 p.m., "Blood Pressure and the Eyes", Dr. E. J. Donaldson; 9.00 p.m., "Blood Pressure and Strokes", Dr. George Selby.

Wednesday, October 28: 8.00 p.m., "Treatment—Selection of Patients", Dr. F. L. Ritchie; 8.30 p.m., "Reserpine and Chlorothiazide", Dr. J. Raftos; 9.00 p.m., "Ganglion-Blocking Agents", Dr. G. E. Bauer.

Each seminar will conclude with a panel discussion, and supper will be served. The inclusive fee for attendance is £1 1s., and early written application, enclosing remittance, should be made to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-8.

Subjects for further evening seminars will include atherosclerosis, ischæmic heart disease, heart failure, heart disease in young subjects, rheumatic heart disease, cardiac investigations, electrocardiography and advances in therapy with appropriate medical films. There will also be two short intensive week-end courses each year in electrocardiography (March) and recent advances in cardiovascular diseases (August). Plans are already well advanced for the establishment of a correspondence course in electrocardiography.

Nominations and Elections.

THE following have applied for election as members of the New South Wales Branch of the British Medical Association:

Sietsma, Anton Samuel Jacobus, M.B., B.S., 1957 (Univ. Sydney), 17 Fitzpatrick Avenue, French's Forest.

White, Peter Wilton, M.B., B.S., 1958 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Bosch, Edward Graham, M.B., B.S., 1958 (Univ. Sydney), 254 Edgecliff Road, Woollahra.

Notes and News.

Royal Australian Army Medical Corps Dinner.

As part of the Annual Corps Day Celebrations for 1959, the officers of the Royal Australian Army Medical Corps, Eastern Command, will hold a dinner at the Imperial Service Club, 11 Barrack Street, Sydney, on Saturday, October 10, 1959. A wreath is to be laid on the Cenotaph at 1815 hours, and officers attending the dinner are requested to assemble outside the Imperial Service Club at 1800 hours. Dinner will be held at 1900 hours. The cost per member will be £2 5s. Dress will be No. 2 walking out or dinner jacket. Units will assist the committee by making "block" reservations and collecting the subscriptions from members of their Officers' Mess. Former members of units who are now on the Retired List or Reserve of Officers may attend.

Further information can be obtained from any of the following committee members: Lieutenant-Colonel R. D. Rothfield, 5 Field Ambulance, Paddington (FA 0455 Ext. 319); Major E. W. Pretty, Eastern Command, Medical and Dental Stores, Maroubra (FJ 1735); Captain A. H. Pritchard, Headquarters, Eastern Command (FA 0455 Ext. 267); and Captain W. F. Oakes, 3 Field Ambulance, Marrickville (LM 0373).

National Health Week.

National Health Week throughout Australia will be from October 18 to 24, 1959. The theme of the week for this year is "Clean Hands for Good Health".

Research Fellowship into Kuru.

As part of the investigations being carried out by the Departments of Medicine and of Genetics in the University of Adelaide into the disease kuru in the eastern highlands of New Guinea, the University has created the position of Research Fellow to carry out genetical and clinical field studies in the area concerned. Further information about this position may be obtained from the Registrar, The University of Adelaide, North Terrace, Adelaide.

Deaths.

THE following death has been announced:

STRACHAN.—James Charles Power Strachan, on August 27, 1959, at Creswick, Victoria.

Diary for the Month.

SEPTEMBER 12.—Queensland Branch, B.M.A.: 4th Branch Convocation; Annual General Meeting.
SEPTEMBER 14.—Victorian Branch, B.M.A.: Finance Subcommittee.
SEPTEMBER 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.
SEPTEMBER 16.—Victorian Branch, B.M.A.: Clinical Meeting at Pathology Department.
SEPTEMBER 16.—Western Australian Branch, B.M.A.: General Meeting.
SEPTEMBER 17.—Victorian Branch, B.M.A.: Executive of Branch Council.
SEPTEMBER 17.—New South Wales Branch, B.M.A.: Clinical Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

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